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A LONG-TERM MORTALITY STUDY OF WORKERS OCCUPATIONALLY EXPOSED TO METALLIC NICKEL AT THE OAK RIDGE GASEOUS DIFFUSION PLANT

Supported by Union Carbide Corporation - Nuclear Division (under contract to the Department of Energy) and INCO, United States, Inc.

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Executive Summary

A LONG-TERM MORTALITY STUDY OF WORKERS OCCUPATIONALLY EXPOSED TO METALLIC NICKEL AT THE OAK RIDGE GASEOUS DIFFUSION PLANT

This study was undertaken to determine whether mortality from respiratory cancer among workers occupationally exposed to airborne metallic nickel at the Oak Ridge Gaseous Diffusion Plant (ORGDP) differed from that of workers at the same plant with no record of occupational exposure to metallic nickel or any nickel compound. Two cohorts were identified; one of 814 nickel-exposed workers and a 1,600-worker control group. Both groups were employed at ORGDP prior to 1954 and data were collected through 1973. The members of both cohorts, therefore, had a minimum follow-up of 19 years. Mortality from respiratory cancer and from other causes was examined in both groups and the data indicated no discernible adverse effect on the nickel workers as compared to the control group.

Previous studies on other nickel compounds, such as impure nickel sulfide (Ni_3S_2), showed significantly increased incidence of cancer of the lung and of the nasal cavities. In the present study, no increased incidence rates of these types of cancer were found in workers exposed to the airborne metallic nickel in the barrier manufacturing operation. This suggests that the proposal by NIOSH to use the generic approach to establish nickel exposure standards is not valid, but rather, that the occupational standards for metallic nickel and its compounds should be considered separately.

During the period from 1948 to 1963, the median nickel concentration for 3,044 routine air samples was 0.13 mg/cu m. In retrospect, evaluation of the air monitoring data reported at that time indicates that the data may be biased toward the low side and the workers probably were exposed to higher concentrations. Current levels of nickel concentrations--under considerably improved work conditions and well within present standards--are higher than the historical data.

The results of the study have failed to demonstrate that airborne metallic nickel is a carcinogen in humans. Although the workers employed in the barrier plant had substantial exposures to airborne metallic nickel, they have experienced no increased risk of developing malignancies of the respiratory system. They actually had fewer deaths from this cause than expected. If airborne metallic nickel is a carcinogen, very high exposures for a long period of time must be required to trigger the malignant process.

ABSTRACT

This study was undertaken to determine whether mortality from respiratory cancer among workers occupationally exposed to metallic nickel at the Oak Ridge Gaseous Diffusion Plant (ORGDP) differed from that of workers at the same plant with no record of occupational exposure to metallic nickel or any nickel compound. A cohort of 814 nickel-exposed workers and one of 1600 controls were identified. The members of both cohorts had a minimum follow-up period of 19 years. Mortality from respiratory cancer and from other causes was examined in both groups. The data showed no evidence of an increased risk of mortality due to respiratory cancer among the nickel-exposed workers. The exposed cohort experienced lower mortality than the controls, both in deaths due to respiratory cancer and in deaths due to all causes, although neither of these differences was statistically significant.

BACKGROUND

Epidemiologic studies conducted in Wales, Canada, Norway, and the Soviet Union have shown a significantly increased incidence of cancer of the lung and of the nasal cavities in workers employed in certain nickel refining operations.[1] The increased risk of developing respiratory cancer was particularly associated with the high temperature oxidation of impure nickel sulfide (Ni_3S_2) by the now-obsolete processes of calcining and sintering. The carcinogen or carcinogens responsible for these increased risks have not been specifically identified inasmuch as the workers were exposed to dusty atmospheres containing several inorganic nickel compounds as well as to known carcinogens such as arsenic and polynuclear aromatic hydrocarbons. However, it is known that workers employed in the calcining and sintering operations were not exposed to airborne metallic nickel. Furthermore, the metal was unlikely to have been a significant atmospheric contaminant in any of the other refining operations associated with an increased risk of respiratory cancer.

The results of animal studies on the carcinogenic effects of exposure to airborne nickel metal are equivocal. No animals have developed tumors following exposure to airborne nickel metal, although metaplastic changes were noted in the lungs of exposed rats and guinea pigs. Hamsters showed no effects attributable to exposure to metallic nickel.[2]

The observation of metaplastic changes in some animals exposed to nickel metal coupled with the assumption that "... air oxidation of fine dusts of nickel metal probably results in inhalation of nickel oxide by workers exposed to airborne nickel metal"[3] has led the National Institute of Safety and Health (NIOSH) to declare that metallic nickel must be considered a suspect carcinogen.

In view of the uncertainty about the carcinogenicity of metallic nickel, it seemed desirable to investigate whether adverse health effects could be detected in humans exposed to metallic nickel dust. Such a group was identified among employees of the Oak Ridge Gaseous Diffusion Plant (ORGDP) of Union Carbide Corporation's Nuclear Division (UCC-ND) in Oak Ridge, Tennessee. In one department of the ORGDP, finely divided, high-purity, metallic nickel powder is used to manufacture "barrier," a special porous medium employed in the isotopic enrichment of uranium by gaseous diffusion. The metallic powder is not oxidized during processing. The present study examines the possible effects of occupational exposure to metallic nickel on the mortality experience of the barrier workers, with particular reference to respiratory cancer.

STUDY DESIGN

This epidemiologic investigation was designed to determine whether mortality due to respiratory cancer was affected by exposure to metallic nickel in the barrier manufacturing environment. To do this, the mortality of workers who were first occupationally exposed to metallic nickel before 1954 was compared with that of workers at the same plant who had no record of any occupational exposure to metallic nickel or to

nickel compounds during their employment at ORGDP. The mortality experience of the exposed and control groups was also compared with that expected in these two cohorts based on the experience of the appropriate subgroups of the United States population.

Selection of Exposed and Control Populations - Manufacture of barrier using nickel powder began at ORGDP in January, 1948. The work histories of 980 ORGDP employees carry a department code indicating they worked in the barrier plant sometime between January 1, 1948, and the end of the study period on December 31, 1972. Since 852 of these 980 workers were hired directly into, or were transferred to, the barrier plant before January 1, 1954, it was decided to study only this pre-1954 group, thereby assuring a potential observation period of at least nineteen years for each exposed individual. All of the 852 employees who worked in the barrier plant before 1954 were whites; 814 of these workers were males and 38 were females. Because of the limited number of female employees, analysis was limited to the white males.

The duration of employment of these 814 white male employees in the barrier plant during the study period ranged from a minimum of three days to a maximum of 25 years, with an average employment period of 5-1/3 years and a median of 3-3/4 years. The distribution of the duration of employment of these employees is shown in Figure 1. There are 653 employees who worked in the barrier plant more than a year, while 71 worked there less than six months, and six of these worked less than one month. In addition to employment in the barrier plant, two-thirds of the 814 men also worked in other departments; 91 were originally hired into the barrier plant and then transferred out; and

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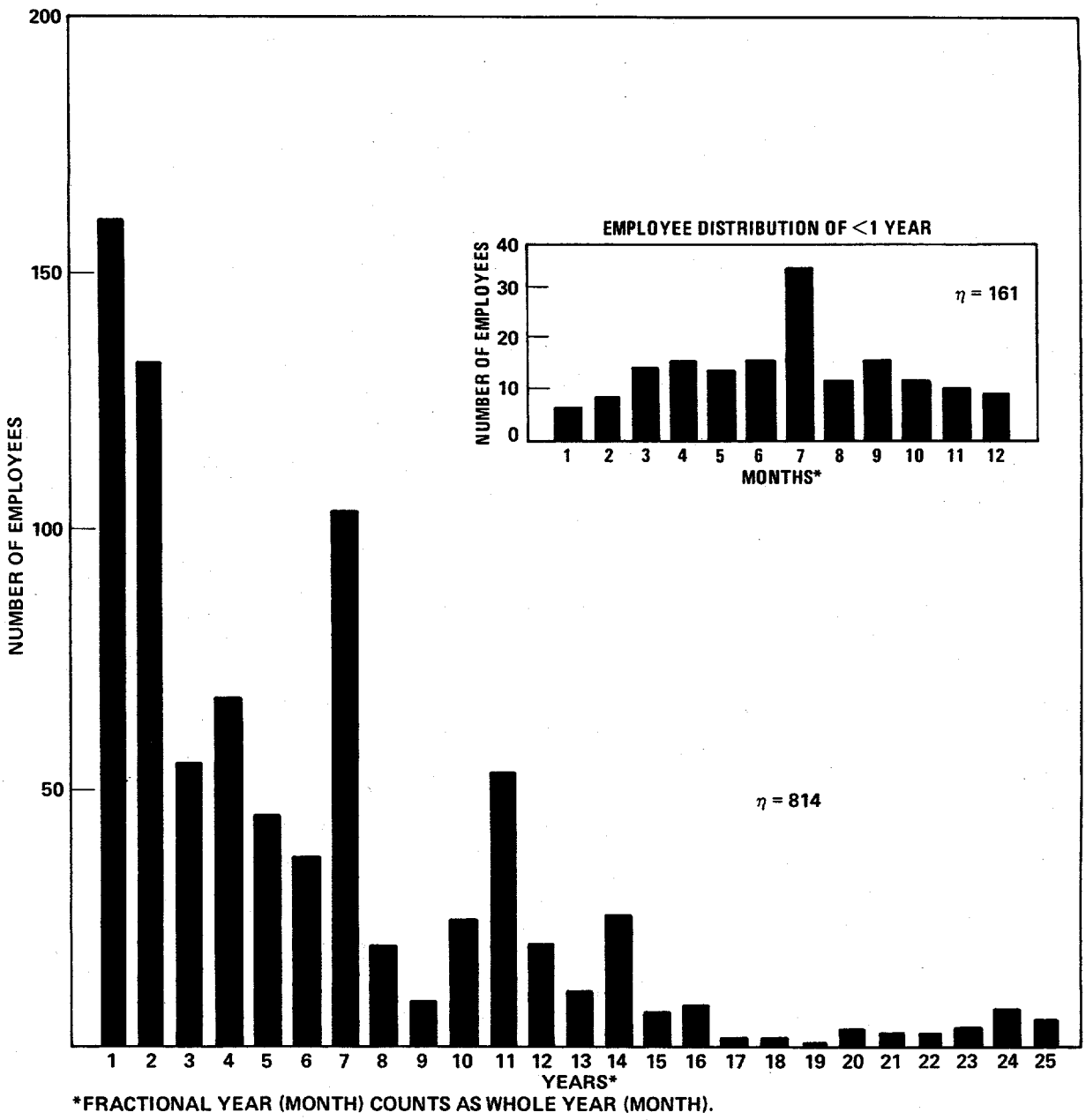

*FRACTIONAL YEAR (MONTH) COUNTS AS WHOLE YEAR (MONTH).

Figure 1

DURATION OF EMPLOYMENT IN BARRIER PLANT

224 worked in other departments before and after assignment to the barrier facility.

The control group was selected from all white male employees at ORGDP who had no record of occupational exposure to metallic nickel or to nickel compounds while employed at ORGDP and whose period of active employment included at least one day in the period January 1, 1948, through December 31, 1953. The employees in this cohort thus had the same potential for being hired into or transferred to the barrier plant during the same time period as did the exposed population. The eligible employees were arranged in order by Social Security number, and every fourth worker was selected. This 25 percent sample yielded exactly 1600 white male workers.

Exposure of Barrier Workers to Airborne Metallic Nickel - Routine air sampling was performed at ORGDP from 1948 to 1963. During this period, 3044 air samples were collected in various areas of the barrier plant and were analyzed for nickel content. The distribution of the concentration of airborne nickel in seven areas of the barrier plant is shown in Table 1. The median nickel concentration for the 3044 samples was 0.13 mg/cu m. The routine sampling program was discontinued in 1964, and air sampling was performed only on an "as-needed" basis for control purposes. Unfortunately, the results of the analyses of these later samples were not retained.

In retrospect, air monitoring data reported as zero probably should have been reported as less than 0.1 mg/cu m. This value was the lowest concentration that could be reliably detected with the sampling and analytical methods routinely used by the plant laboratory at the

TABLE 1

AIR MONITORING IN BARRIER PLANT (1948-1963)

Area	Number of Samples[1]	Concentrations in mg Nickel/cu m						Distribution of Workers
		Minimum[2]	Lower Quartile[2]	Median[2]	Upper Quartile	90th Percentile	Maximum	
Manufacturing Area 1	2220	0	0	0.10	0.56	1.80	566.0	30%
Manufacturing Area 2	219	0	0.17	0.50	4.80	27.10	459.0	4
Manufacturing Area 3	213	0	0	0.10	0.70	1.40	140.8	39
Manufacturing Area 4	17	0	0	0	.05	.44	1.0	5
Material Recovery Area 1	332	0	0	0.10	0.60	1.24	103.1	4
Material Recovery Area 2	30	0	0	0.10	0.30	0.95	7.1	5
Laboratory Area	13	0	0	0.03	0.40	37.99	62.9	12

[1] Generally limited period samples of approximately 30 minutes

[2] Data reported as 0 include all values less than 0.10 mg Ni/cu m
(Note page 5 of text)

time. Under considerably improved working conditions, current levels of nickel concentrations collected by industrial hygiene personnel are higher than historical data.[4] Therefore, it is reasonable to assume that the reported median of 0.13 mg/cu m is biased toward the low side. The accurate reporting of data in the 0 to 0.1 mg/cu m range would have had the general effect of increasing the observed lower quartile concentration of airborne metallic nickel in the work areas.

In 1957, a program of biological monitoring (urinalysis) was implemented in the barrier plant. From this program, urinary nickel concentrations are available for 238 of the 814 barrier workers included in this study, but the analytical methods that were used have subsequently been shown to be of questionable specificity, with particular sensitivity to iron contamination. In a summary of nickel urinalysis data reported from ten other studies, the highest mean concentration was 40μ g/l.[1] However, well over 75 percent of the nickel concentrations determined in the urine of barrier workers was between one and two orders of magnitude greater than this. Consequently, the urinalysis data have not been used to evaluate exposure to nickel in this investigation.

The employment histories of the workers did not specify the area in the barrier plant to which the individual was assigned. It is also known that workers were frequently moved from one area of this plant to another. Thus, it is not possible to associate individuals with specific areas of exposure. However, the operation of the plant was such that the distribution of the total work force into the various work

areas remained reasonably constant. An estimation of this distribution is shown in the last column of Table 1. About 70 percent of the work force was assigned to areas one and three with the remaining 30 percent divided among the other five work areas.

Although the distinguishing characteristic of the exposed workers as compared to the controls was their employment in the barrier manufacturing plant, it should be pointed out that workers in both groups had opportunity for occupational exposure to environmental agents other than nickel. Inasmuch as two-thirds of the barrier workers also worked in other departments of the ORGDP, their exposure to other substances was similar to that experienced by the controls. However, nickel was the only substance in the barrier plant for which exposure was limited to that particular location. No effort was made in this investigation to evaluate the possible health effects in these workers of exposures to agents other than nickel.

Ascertainment of Mortality Status - In order to make a comparison of mortality in the exposed and control cohorts, it was necessary to follow each worker in the two groups from the date of initial hire to death or to the termination of the study period. At the time this investigation was initiated, all workers who had ever been employed at ORGDP were already enrolled in the larger population of the ongoing ERDA Health and Mortality Study.* The availability of data on the

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*This study was conducted by Dr. Thomas F. Mancuso from June, 1964, through July, 1977, under contract No. E(11-1)-3428 for the United States Energy Research and Development Administration.

mortality status of all ORGDP employees greatly facilitated this investigation.

Early in 1974, a roster of all former workers who were no longer employed at ORGDP as of January 1, 1974 was sent to the Social Security Administration (SSA). From their records, SSA determined which individuals had paid Social Security taxes in the last quarter of 1973 or had been paid retirement or disability benefits in December, 1973. The SSA records of the remaining workers were then searched for evidence of death of the worker and the names of the individuals who had died were furnished to the staff of the ERDA Health and Mortality Study. In addition, the date of death and the city and state where the claim for death benefits was filed were provided for non-annuitants. For annuitants, SSA identified the month and year the last benefit check was paid, and the state to which it had been mailed. In mid-1974, the search for death certificates for these individuals began.

There can be several months delay between the receipt of information about the death of an individual at the local level and the transmission of this information to the central files of the SSA. To assure as complete ascertainment of deaths as possible through the SSA, only the deaths which occurred before 1973 were included. Thus, the observation period for this study was from January 1, 1948 through December 31, 1972.

The roster of non-current employees of ORGDP which was sent to SSA early in 1974 included the names of 745 former employees of the barrier plant (69 were still employed at ORGDP as of January 1, 1974) and 1397 names of former employees of other departments at ORGDP who

were subsequently selected as controls for this study (203 controls were still employed). SSA identified 86 deaths which had occurred before 1973 among the 814 barrier workers and 273 deaths among the 1600 controls. Death certificates for 83 of the barrier workers and 255 controls were already on file in the ERDA Health and Mortality Study office when the present investigation was initiated. At that time, the search for the 21 death certificates not yet located was intensified.

The SSA had provided information that one of the barrier workers without a certificate was a casualty of the Vietnam War. The Department of Defense could not locate the records for this man without a military service number, so it has not been possible to obtain this certificate. The death has been classified as a military casualty for purposes of analysis. One of the deceased control workers without a certificate was in Spain when he died, and his death certificate was obtained through the State Department. The information on the remaining 19 workers identified as dead was sent to the appropriate offices of the 50 states with a request for a search for certificates for the listed individuals. At this time, certificates have been received for the remaining two deceased barrier workers and seven of the deceased control workers. All but five states responded to the request for a search, and there is no ready explanation for the failure to locate eleven of the certificates for deceased control workers.

MORTALITY ANALYSIS

Each available death certificate was coded as to the underlying cause of death in accordance with the International Classification of

Disease revision current at the time the death occurred. The observed deaths, distributed according to the underlying cause, for the barrier workers and for the control population, are shown in Table 2. The 11 deaths among the controls for whom death certificates have not yet been obtained have been distributed among the causes of death in the same proportions as the 262 deaths of controls for whom certificates were available. This procedure resulted in the fractional numbers of "observed" deaths among the controls.

The members of the control population were older than those of the exposed group and, thus, were at greater risk during the observation period. This difference between the cohorts was adjusted for by calculating the deaths to be expected in each cohort as though it had experienced the same mortality as the population of U.S. white males.

The man years at risk for each calendar year 1948 through 1972 were calculated by five-year age groups. The members of the barrier worker cohort became at risk on the date they were first employed in the barrier plant. The members of the control cohort became at risk on the date they were first employed at ORGDP or on January 1, 1948, whichever was later. Each worker in both cohorts ceased contributing to man years at risk on the date of his death or on December 31, 1972, whichever was earlier. The 814 barrier workers accumulated 17,232 man years at risk, 26 per cent of which were spent in employment in the barrier plant; and the 1600 controls accumulated 34,701 man years. (The tables of man years at risk for the two cohorts are attached as Appendixes I and II.) The expected number of deaths for each cohort was calculated by applying the appropriate age-, year-, and cause-

TABLE 2

OBSERVED AND EXPECTED DEATHS BY CAUSE FOR THE EXPOSED AND CONTROL COHORTS (1948-1972)

	Barrier Workers		Controls	
	Observed	Expected	Observed	Expected
ALL CAUSES	85*	112.81	273.00	325.81
Infective and Parasitic Diseases	-	1.73	2.08	5.54
Malignant Neoplasm	19	20.25	48.89	60.41
Buccal Cavity and Pharynx	3	0.73	1.04	2.14
Digestive Organs and Peritoneum	3	5.47	10.40	17.79
Respiratory System	3	6.68	21.85	19.42
Bone, Connective Tissue, Skin, and Breast	2	0.77	1.04	1.91
Genitourinary Organs	3	1.86	4.16	6.64
Other and Unspecified Sites	2	2.24	5.20	5.56
Lymphatic and Hematopoietic	3	2.50	5.20	6.46
Benign Neoplasm and Neoplasm - Nature Unspecified	1	0.40	-	1.03
Endocrine, Nutritional, and Metabolic Diseases	4	1.88	1.04	5.45
Diseases of Blood and Blood-Forming Organs	-	.24	2.08	0.73
Mental Disorders	-	.82	2.08	1.84
Diseases of Nervous System and Sense Organs	-	1.14	2.08	2.89
Diseases of Circulatory System	34	52.70	149.80	167.91
Diseases of Respiratory System	5	5.31	14.56	16.99
Diseases of Digestive System	3	6.90	1.04	18.07
Diseases of Genitourinary System	1	1.58	6.24	4.90
Diseases of Skin and Subcutaneous Tissue, Musculo-Skeletal System, Connective Tissue, and Congenital Anomalies	-	0.70	-	1.65
Symptoms and Ill-Defined Conditions	6	1.36	7.28	3.57
Accidents, Poisonings, and Violence	12	17.78	35.37	37.81

* An additional barrier worker was a Vietnam war casualty.

specific mortality rates for the U.S. white male population[5] to the age- and year-specific man years at risk in the two study populations. The sums of these products are shown in Table 2 under the heading Expected Deaths for each population of workers.

Mortality from All Causes of Death - Based on the U.S. white male population, both the exposed and control cohorts have experienced lower mortality from all causes than expected, and these differences are statistically significant. The Standard Mortality Ratio (SMR = observed deaths divided by expected deaths) for all causes of death in the barrier workers is 0.75, and its 95 percent confidence interval is (0.60, 0.94). The SMR for all causes of death in the controls is 0.83 (0.74, 0.94). The similarity in overall mortality between these two cohorts suggests that both groups of workers are comparable with respect to the underlying force of mortality.

As stated earlier, 38 white females were employed in the barrier plant at some time between 1948 and 1953. Although these workers have not been included in these analyses, the mortality status of these women was determined as part of the ERDA Health and Mortality Study. Only one of these early female workers has died, and the cause of her death was cancer of the liver.

Mortality Due to Malignancies of the Respiratory System - Malignancies of two sites have been associated with workers in certain nickel refining operations: the lung and the nasal sinuses. All identified malignancies of the respiratory system in the workers included in this study were of the lung, 3 in the barrier workers and 21 in the controls. The expected number of deaths from lung cancer were calculated using

the rates of all observed deaths in white males in the U.S. which were coded to ICD 47 during the 5th revision, to 160-165 during the 6th and 7th revisions, and to 160-163 during the 8th revision. The SMR for malignancies of the respiratory system is 0.45 (0.09, 1.31) for the barrier workers and 1.13 (0.71, 1.71) for the controls, a difference which is not statistically significant. The number of deaths from this cause in either cohort does not differ statistically from the number of deaths expected for that cohort.

Mortality Due to Other Causes - Several other observations on the data in Table 2 are worth mentioning. In no cases does the mortality of the barrier workers differ statistically from that of the controls. However, for two causes of death the mortality experience of the barrier workers is significantly different from the expectations based on U.S. white males. The barrier workers had a deficiency of deaths due to Diseases of the Circulatory System with an SMR of 0.65 (0.24, 0.90). Also, they had an excess of deaths due to Symptoms and Ill-Defined Conditions (SMR= 4.41 [1.62, 9.61]). The deaths included in this latter category were all sudden or unattended deaths.

The control cohort had one death due to Diseases of the Digestive System as compared to the 18 expected. For this cause of death, the observed number is significantly low with an SMR of 0.06 (0.00, 0.33).

The directional consistency of the observations in the two cohorts for all three of these causes of death suggests that the deviations from expectancies reflect conditions affecting the total ORGDP work force rather than any occupational subgroup. The deficiencies in deaths from Diseases of the Circulatory System may result from the extensive

program in occupational medicine which has been in operation at ORGDP since the plant opened.

The excess of deaths undefined as to specific cause of death probably reflects the absence of a law in Tennessee making autopsy mandatory in the case of sudden or unattended deaths. If a person does not have a private physician at the time of sudden death and no autopsy is performed, the cause of death recorded on the certificate is simply "Natural Causes."

There does not seem to be any simple explanation for the very few deaths resulting from Diseases of the Digestive System in these two cohorts. It is beyond the scope of this investigation to probe further into this finding, but this interesting observation probably warrants additional investigation.

INTERPRETATION OF FINDINGS

This investigation provides no evidence to support a hypothesis that exposure to airborne metallic nickel has increased the risk of death in barrier workers due to malignant neoplasms of the respiratory system. In fact, although the differences are not statistically significant, the barrier workers had relatively fewer deaths from respiratory malignancies than did the workers who were not exposed to metallic nickel, as well as having fewer deaths than predicted by the experience of all U.S. white males. A reasonable question to ask is whether there is any reason to suspect that the in-plant control group and the U.S. white male population should be expected to have a higher underlying risk of dying from respiratory cancer than the barrier cohort.

All members of both worker populations were employed in the same industrial complex and, therefore, lived in the same geographical area at some time during the six-year period 1948-1953. As the greater part of each population had been employed for more than a year, with more than half of the workers in both groups having periods of employment at ORGDP exceeding 10 years, these two groups of workers probably experienced similar life styles and environmental impacts for a significant part of their adult lives. Also, since two-thirds of the barrier workers had work experience in other departments at ORGDP, the assumption that most of the barrier workers had been exposed to occupational stresses similar to those of the controls seems valid. The fact that the overall mortality, adjusted for age and calendar-year differences, in both groups is so similar adds credence to the validity of these assumptions.

Any study which investigates the occurrence of respiratory malignancies must consider the possible compounding effects of the recognized carcinogen, cigarette smoke.[6] The medical records of the employees are the only available source of information about their smoking habits. At the time of initial hire of each individual in this study (i.e., on or before December 31, 1953), no question concerning smoking habits was asked for the medical record. However, in 1955 the use of the Cornell Medical Index Health Questionnaire was instituted, which contained the question, "Do you smoke more than 20 cigarettes a day?" For each employee in the study, the first response to this question appearing in his medical record was abstracted. No information on smoking is available for employees who terminated before the Cornell Questionnaire was

used. The percentage distribution of responses for the two groups is shown in Figure 2. From these data, it is seen that the two groups are comparable in the percentage answering the question, "Yes," but that more barrier workers than controls answered the question, "No." This difference is compensated for by a higher percentage of controls having an unknown smoking history. If those persons for whom smoking histories were not available were similar in their smoking habits to those for whom smoking histories were available, there would have been a smaller proportion of smokers in the barrier workers than in the control population; however, there is no justification for this assumption. If such were the case, this could account for some of the deficit in respiratory malignancies in the barrier group. Recognizing that smokers have an increased risk of developing diseases of the circulatory system, the SMR of 0.65 for this cause of death in the barrier workers as compared to 0.76 in the controls is consistent with fewer smokers in the barrier cohort. However, the difference in mortality between barrier workers and controls due to diseases of the circulatory system does not appear to be large enough for smoking patterns to explain all the deficit in observed deaths due to respiratory malignancies in the barrier workers.

The mortality experience of the U.S. white male population predicted more deaths than occurred in either of the study cohorts. There are at least three possible explanations for this observation. The first possible explanation is the so-called "healthy-worker effect," i.e., an effect due to selection on the basis of health, current or past. As McMichael et al.[7] point out, "This selection process only

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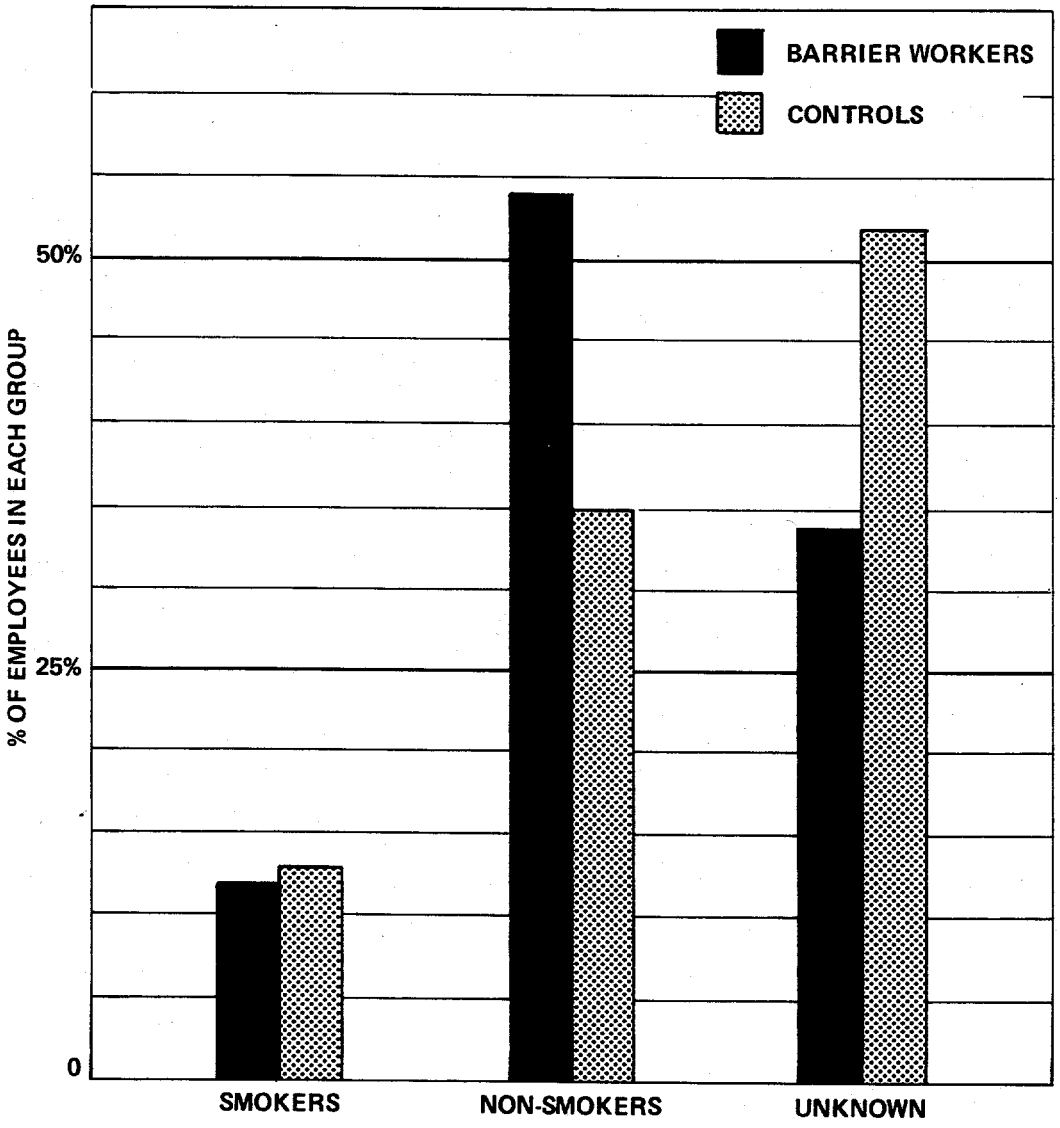

Figure 2
SMOKING HISTORIES OF BARRIER WORKERS AND CONTROLS

directly affects active workers...(showing) a decline in effect with the passage of time beyond cohort identification." Since, in this study, follow-up is not a function of active employment beyond cohort identification, there is little reason to suspect that the "healthy-worker effect" has contributed significantly to the lower-than-expected mortality. The second is the possibility of under-reporting of deaths by Social Security. The third is the active occupational health program which has been in effect at ORGDP since the opening of the plant. However, it is quite probable that these three factors have all contributed in some degree to the observed results.

Use of U.S. death rates resulted in the prediction of fewer deaths from malignancies of the respiratory system than were observed in the control group (19.42 expected vs. 21.85 observed) and more than twice as many deaths as were observed in the exposed workers (6.68 expected vs. 3 observed). Thus, it does not appear that the factors which caused a reduction in the overall mortality in the controls when compared with U.S. data were operating to the same extent for mortality due to respiratory malignancies. Therefore, it seems reasonable to accept the premise that the U.S. data should adequately predict the respiratory malignancy deaths to be expected in the barrier workers. The validity of using U.S. statistics to calculate these expectancies in the ORGDP workers is further supported by the fact that for the years 1950-1969, the lung cancer mortality rates for white males in Anderson and Roane counties, Tennessee, the counties in which Oak Ridge is situated, were very nearly equal to the national rates.[8]

There does not seem to be any evidence to suggest that either the in-house controls or the U.S. white male population should have different underlying risks of dying of respiratory cancer from the workers in the barrier plant. If airborne metallic nickel is a carcinogen, why have the barrier workers not shown an effect due to their occupational exposure? One possible explanation is that they have not been followed long enough for the effect to become evident. Another possibility is that the length and degree of their exposures were not sufficient to cause the effect.

Every worker included in the cohort exposed to metallic nickel had a potential follow-up period of at least 19 years and at most 25 years from his first date of employment in the barrier facility. Although the barrier workers were a relatively young group when they were hired, the lengthy observation period allowed this population to age so that 11 percent of the man years of observation were for ages of 55 and over. These are the ages at which the incidence of lung malignancies in U.S. white males reaches its peak. Thus, if exposure to airborne metallic nickel increased the underlying risk of developing lung tumors, it should have begun to appear at least in the older workers. There are few data available on the latency period between exposure and death in the epidemiologic studies of nickel refining workers which have been reported. Data adapted from the study of the workers at a nickel refinery in Kristiansand, Norway by Pedersen et al.[9] reported a range of 4 to 47 years as the interval between start of employment and diagnosis of lung cancer. Even if a normal distribution is assumed for these intervals, any excesses should start to appear by 20 years after

exposure; and yet the workers in this study are not only showing no excess of cases, but have a deficit of cases. Insufficient follow-up time after exposure, therefore, does not appear to be a reasonable explanation for the observations in this study.

Exposure data for the nickel refinery workers are imprecise or nonexistent, particularly for the early cohorts which had very high rates of respiratory cancer. Furthermore, the refinery workers were usually not exposed to airborne metallic nickel. Thus, it is impossible to compare exposure levels of the barrier workers with those of the early refinery workers. The present U.S. standard for workplace exposure to nickel metal is an eight-hour Time Weighted Average concentration limit of 1 mg/cu m. The standard which has been recommended by NIOSH is 0.015 mg/cu m for up to a ten-hour period.

All of the barrier workers included in this investigation were employed at some period between 1948 and 1963 when the air monitoring program was in effect at ORGDP. As can be seen in Table 1, most of the workers in the barrier plant were exposed to levels of nickel concentration higher than the current standard. Ninety percent of the workers were exposed to levels greater than 1 mg ten percent of the time, and 82 percent of the workers were exposed to 0.10 mg/cu m or more 50 percent of the time. Most of the air samples were thirty-minute collections. With this sampling time and the analytical methods in use at that time, the minimum, reliably detectable, nickel concentration in air was 0.10 mg/cu m; therefore, it can be assumed that all of the workers were exposed to levels greater than the recommended NIOSH standard of .015 mg/cu m during most of the work day. Although some short-term employees

have been included in this study, 743 men worked in the barrier plant more than six months, and 407 worked more than three years nine months in the facility. Thus, the workers in this study appear to have had substantial exposures to airborne metallic nickel.

CONCLUSION

This investigation was undertaken to determine if it could be demonstrated that airborne metallic nickel is a carcinogen in man. The study has failed to do this. Although the workers employed in the barrier plant had substantial exposures to airborne metallic nickel, they have had no increased risk of developing malignancies of the respiratory system. They actually had fewer deaths from this cause than expected. If airborne metallic nickel is a carcinogen, very high exposures for a long period of time must be required to trigger the malignant process.

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ACKNOWLEDGMENTS

The authors wish to acknowledge the contributions of the following people to the material that was necessary to generate this report: Dr. C. W. Weber and his staff, A. Estes and P. G. Corley; Dr. T. G. Fortney; R. D. Gilmore; S. S. Stief; and M. E. Mitchell. Appreciation is also expressed to the medical departments and records management organizations of the four Union Carbide Nuclear Division (UCC-ND) plants. A special debt is owed H. L. Fore and the Computer Sciences Division of UCC-ND for coordination and advice on matters of computerized records storage; much of the computer work is attributed to H. L. Fore and L. F. Denton of UCC-ND. The assistance of Tom Akin of the Oak Ridge Associated Universities Computer Center in generating the expected mortality data is also acknowledged.

Certain data used in this publication were derived from statistics furnished by the Social Security Administration. The authors did not at any time have access to any information relating to specific individuals or reporting units. The authors assume full responsibility for the analysis and interpretation of the data.

APPENDIX I

Man Years at Risk, By Age Group and Year, for Barrier Worker Cohort

Year \ Age	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	≥ 75	Total
1948	0	5	7	3	2	5	0	1	1	0	0	0	0	24
1949	1	23	37	43	40	26	9	9	4	0	0	0	0	192
1950	2	29	70	68	67	39	14	13	3	1	0	0	0	306
1951	2	47	97	94	95	56	28	13	7	1	0	0	0	440
1952	4	57	136	129	112	72	32	13	9	3	0	0	0	567
1953	3	88	210	172	147	82	41	16	12	3	0	0	0	774
1954	1	66	213	196	149	98	51	20	12	5	0	0	0	811
1955	0	47	183	201	166	110	61	23	14	5	1	0	0	811
1956	0	24	153	208	181	123	69	31	14	7	1	0	0	811
1957	0	10	124	217	183	133	82	34	13	9	3	0	0	808
1958	0	3	93	223	182	150	83	41	16	12	3	0	0	806
1959	0	1	65	213	195	146	97	50	20	12	4	0	0	803
1960	0	0	47	182	199	164	108	59	23	14	4	1	0	801
1961	0	0	24	152	206	178	121	66	31	13	6	1	0	798
1962	0	0	10	124	216	179	129	78	33	12	8	3	0	792
1963	0	0	3	93	223	177	147	81	39	16	10	3	0	792
1964	0	0	1	65	212	191	143	94	48	20	9	4	0	787
1965	0	0	0	47	182	194	162	104	56	22	11	3	1	782
1966	0	0	0	24	152	204	174	117	63	27	12	4	1	778
1967	0	0	0	10	124	214	178	123	76	29	11	6	3	774
1968	0	0	0	3	93	221	173	140	78	36	15	7	3	769
1969	0	0	0	1	65	211	186	136	91	47	16	8	4	765
1970	0	0	0	0	47	181	188	155	100	53	19	11	4	758
1971	0	0	0	0	24	150	201	165	111	56	24	12	5	748
1972	0	0	0	0	10	123	210	169	115	67	24	11	6	735
Total	13	400	1473	2468	3272	3427	2687	1751	989	470	181	74	27	17232

APPENDIX II

Man Years at Risk, By Age Group and Year, for Control Cohort

Year \ Age	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	≥ 75	Total
1948	0	85	177	212	159	123	87	46	35	21	1	0	0	946
1949	0	61	185	212	169	132	99	48	38	22	6	0	0	972
1950	0	35	188	205	207	141	100	64	40	20	10	0	0	1010
1951	2	39	182	228	230	151	113	75	37	30	12	0	0	1099
1952	14	70	227	267	265	177	136	84	41	29	18	0	0	1328
1953	9	115	238	308	284	207	150	96	48	33	20	1	0	1509
1954	1	111	221	330	284	221	169	110	51	36	18	6	0	1558
1955	0	85	188	337	264	260	173	113	69	38	16	9	0	1552
1956	0	57	164	312	289	268	183	124	79	36	24	10	0	1546
1957	0	35	144	286	302	279	195	138	83	39	23	13	0	1537
1958	0	12	132	253	313	282	212	147	94	41	27	14	0	1527
1959	0	1	110	220	329	282	215	164	107	42	33	11	3	1517
1960	0	0	84	187	336	261	253	167	110	61	34	10	5	1508
1961	0	0	57	164	309	285	260	176	120	69	32	18	6	1496
1962	0	0	35	144	283	299	269	190	131	72	34	19	9	1485
1963	0	0	12	132	251	308	276	205	138	84	35	25	10	1476
1964	0	0	1	110	220	324	275	206	155	96	35	32	8	1462
1965	0	0	0	84	186	331	256	241	161	100	50	31	8	1448
1966	0	0	0	57	162	305	279	248	171	111	58	28	15	1434
1967	0	0	0	35	143	280	294	256	186	120	64	27	17	1422
1968	0	0	0	12	132	248	304	261	199	130	71	30	22	1409
1969	0	0	0	1	110	216	319	263	199	149	80	30	25	1392
1970	0	0	0	0	84	184	326	246	231	156	84	43	25	1379
1971	0	0	0	0	57	162	299	270	237	160	94	49	29	1357
1972	0	0	0	0	35	143	275	283	242	170	101	53	30	1332
Total	26	706	2345	4096	5403	5869	5517	4221	3002	1865	980	459	212	34701

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K/NI-1, Part 1

PROJECT PROGRESS REPORT FOR JANUARY 1977 NIOSH STANDARDS EVALUATION OF NICKEL POWDER

C. W. Weber
Manager, NIOSH Standards Evaluation Project

J. C. White
UCCND Technical Services Manager

February 1, 1977

UNION CARBIDE

OAK RIDGE GASEOUS DIFFUSION PLANT
OAK RIDGE, TENNESSEE

prepared for the **U.S. ENERGY RESEARCH AND DEVELOPMENT ADMINISTRATION**
under **U.S. GOVERNMENT** *Contract W-7405 eng 26*

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HIGHLIGHTS

This is the first in a series of progress reports on a study of K-25 personnel who have worked in areas where nickel powders were used and handled. The project was initiated to evaluate the health effects of handling nickel powder and to help in determining whether a recent NIOSH proposal to reduce tolerable airborne nickel levels by a factor of 200 is necessary with regard to elemental nickel.

During January the basic organization of the project was completed, staff briefings were held, and studies were commenced on the personnel data and environmental exposure data available.

[redacted]

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PROJECT PROGRESS REPORT FOR JANUARY 1977
NIOSH STANDARDS EVALUATION OF NICKEL POWDER

INTRODUCTION

The National Institute of Occupational Safety & Health (NIOSH) is currently proposing to reduce the tolerable airborne levels for nickel by a factor of 200, down to the level of 5 µg/cu m. The International Nickel Corporation (INCO), ERDA, and UCCND are very concerned with this proposal and have discussed the possibility of conducting an epidemiologic study of K-25 personnel who have worked in areas where nickel powder was used and handled. Similar studies have been made by INCO; however, it was not feasible to exclude exposure to other nickel compounds and impurities. An objective study at K-25 could provide data uniquely isolating elemental nickel, which might be used to better establish the health effects of nickel powder exposure. INCO has proposed to share the costs of the study.

Following a general discussion in December, 1976, of such a study at K-25, this project was initiated with the following objective: to organize and conduct a study of K-25 employees who have worked in areas where nickel powder was used or handled, in an effort to evaluate the health effects of such work. This project includes an epidemiologic study of K-25 nickel workers, with an examination of environmental exposures and associated industrial hygiene monitoring.

PROJECT ORGANIZATION

Dr. C. W. Weber was appointed Project Manager reporting to Dr. James C. White, UCCND Technical Services Manager. Other participants presently appointed to the project are: Dr. T. G. Fortney, Medical; Mr. R. D. Gilmore, Industrial Hygiene; Mr. M. E. Mitchell, K-25 Environmental Management; and Dr. E. D. Tompkins, Epidemiologist. Dr. Tompkins is a member of the ORAU (Oak Ridge Associated Universities) staff, specifically the Medical and Health Sciences Division; she is Q-cleared, familiar with many of the K-25 and ERDA organizations involved, and is presently available for this project. Other epidemiologists of national reputation may be consulted later to review and offer critique of our progress and final report.

Other project support will include an ORAU biostatistician, computer personnel, clerical help, analytical and environmental help, and possibly others.

EPIDEMIOLOGIC STUDY

The existence of relevant data on a group of about 2500 nickel workers was identified at the UCCND Computer Technology Center (CTC). ERDA has arranged to release pertinent data on this test group to Dr. E. D. Tompkins. Two computer printouts have been received from CTC. One is a listing of the approximately 2500 UCCND workers ever exposed to nickel, giving for each worker the Name, Social Security Number, Birthdate, Sex, Race, Work locations, Year beginning each work location, and Job description. Review of this listing revealed that only about 40% of these workers have worked in the K-25 Barrier Plant. The second printout from CTC gives a more detailed work history of the approximately 1000 workers who have ever worked in the Barrier Plant. Information from these printouts is presently being used to calculate the number of employee-years-of-exposure received by workers in powdered nickel (barrier) operations. The employee-years-of-exposure are being identified with appropriate calendar years in order to take into account changes that have occurred in the production process.

Additionally, the applicable K-25 employee data are being scoped to establish the total number of employee-years-at-risk. The two parameters, employee-years-of-exposure and employee-years-at-risk, will be used to make some early statistical judgments about the test group. A worthwhile epidemiologic study is not feasible if these aspects are too limited. The scoping calculations will soon be completed.

Of particular interest in this study will be the mortality rates and causes of death of former nickel workers. Special attention will be given cancerous diseases, particularly lung and sinus cancer. The long latency periods for these diseases will require that the emphasis be placed on employment prior to 1956. This further reduces the number of employees in the major test group and the pertinent years-of-exposure and years-at-risk.

A listing of deaths that have occurred in the population of 1000 nickel workers has been requested from CTC. Following review of this information, death certificates will be obtained and examined for causes of death.

Upon completion of the above tasks, a determination can be made either to propose a formal epidemiologic study or to state why such a detailed study would not be warranted.

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ENVIRONMENTAL EXPOSURE

In parallel with the work on the computerized employee work histories, information is being collected from CTC banks, storage in Plant Record vaults, and recent Industrial Hygiene records, which will aid in defining the conditions and levels of employee exposure. These data will include air monitoring and personnel urinalysis values for nickel. Examination of the air monitoring data related to the nickel working environments reveal frequent prevailing conditions in some areas and excursions in others, at concentrations appreciably greater than 5 µg/cu m, the tolerable airborne nickel level recently proposed by NIOSH.

In addition to the study of nickel working environments, two other atmospheric nickel studies were undertaken. One study involved data collected over the past five years within the confines of K-25. The other consisted of collecting and analyzing a limited number of atmospheric samples from five different regions of East Tennessee, in several directions from K-25. The plant data, representing sites located approximately north, south, east, and west of the center of the plant, revealed atmospheric nickel levels ranging from < 0.004 to > 6.0 µg/cu m.

Based on the limited number of off-site samples, the atmosphere in the vicinity of K-25 contains greater nickel concentrations than in surrounding East Tennessee regions. The samples collected from areas remote to K-25 contained nickel concentrations ranging from < 0.004 to ~ 0.13 µg/cu m.

It is apparent, therefore, that the working environments for those handling nickel powder, and also occasionally the general plant environments outside of the Barrier Plant but within the confines of K-25, exceed the level of 5 µg/cu m of nickel, proposed by NIOSH as a new maximum tolerance for airborne nickel.

COORDINATION AND CONTROL

The project study group has visited the Barrier Plant and plans additional briefing and tours. More complete information will be received relevant to work history of specific employees and nickel exposure conditions.

Assuming a complete epidemiologic study will be conducted, an appropriate control group will be identified, probably from either unexposed K-25 employees, or UCCND employees at other sites.

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A special account has been set up for collecting costs of this project. Following mutual agreement concerning the scope and estimated cost of ORAU assistance, a special order will be issued covering the funding authorization.

A program of billing to INCO will be initiated following execution of a formal agreement with that company.

Monthly progress reports will continue to be generated on this project to inform management at ERDA-ORO, K-25, and INCO. These organizations will also participate in the review of the final report of this study.

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PROJECT PROGRESS REPORT FOR FEBRUARY 1977
NIOSH STANDARDS EVALUATION OF NICKEL POWDER

C. W. Weber
Manager, NIOSH Standards Evaluation Project

J. C. White
UCCND Technical Services Manager

March 1, 1977

UNION CARBIDE

OAK RIDGE GASEOUS DIFFUSION PLANT
OAK RIDGE, TENNESSEE

prepared for the **U.S. ENERGY RESEARCH AND DEVELOPMENT ADMINISTRATION**
under **U.S. GOVERNMENT** *Contract W-7405 eng 26*

HIGHLIGHTS

This is the second in a series of progress reports on an epidemiologic study of K-25 employees who have worked with nickel powders, initiated to evaluate health effects of such work.

From project results to date, there is no evidence of increased risk of respiratory malignant diseases as a result of employee exposure to airborne dusts of elemental nickel powders. While these results are limited statistically by the relatively small population under test, the epidemiology study will be conducted and the findings are expected to be available for publication this calendar year.

Preliminary project study has revealed the possibility of other health problems which may or may not be related to exposure to nickel powder and which should be explored through additional epidemiologic investigation.

PROJECT PROGRESS REPORT FOR FEBRUARY 1977
NIOSH STANDARDS EVALUATION OF NICKEL POWDER

INTRODUCTION

This project was initially organized to conduct an epidemiologic study of K-25 employees who have worked in areas where nickel powder was used or handled, in an effort to judge whether such work, with attending elemental nickel powder exposure, leads to health problems, specifically increased incidence of respiratory malignancies. The stimulus for this study is the concern by ERDA-ORO, K-25, and the International Nickel Corporation (INCO) for a current recommendation by the National Institute of Occupational Safety and Health (NIOSH) to reduce the present standard for airborne levels of nickel by a factor of 200, to 5 µg/cu m. Elemental nickel has been included in that proposal, although no studies have been able to isolate exposure to elemental nickel from exposure to nickel compounds and impurities known to be associated with increased incidence of respiratory malignancies.

Because of the long-term use of pure nickel in the manufacture of barrier at K-25, this project can uniquely isolate the effects of exposure to nickel powder (elemental). A significant resource for this study is the data bank of information at the UCCND Computer Technology Center (CTC), which has been collected for the ERDA Health and Mortality Study (H&MS). These files include details of employee work histories for all K-25 employees and the dates of death of any employees known to have died before 1974.

Mrs. E. A. Tompkins, Epidemiologist, is the principal investigator in this study, assisted by Dr. J. H. Godbold, Biostatistician. Both are Q-cleared and on the staff of ORAU (Oak Ridge Associated Universities). Their work to date, using selected ERDA H&MS information from CTC, is the basis for most of this report, the second in the series on this project.

EPIDEMIOLOGIC STUDY: RESPIRATORY MALIGNANCIES - E. A. Tompkins & J. H. Godbold

A review was completed to determine if a sufficient population of workers exposed to nickel powder exists to permit a meaningful epidemiologic

investigation. The documents used in this review were supplied by the Computer Technology Center, from data which had been gathered for the ERDA H&MS. The three documents are: (1) A listing of 2589 workers with potential or known exposure to nickel as a metal or in compound form. For each individual on the list, the following information is available: social security number, date of birth, race, sex, job code, year of entry into each job code, and job title. (2) A detailed work history of each of the 990 workers who had been employed in the Barrier Plant through 1973. This listing provided information on hires, changes in job classification or job code, and termination with dates of each action. (3) A listing of the 175 individuals, among the 2589 "nickel" workers, whom the Social Security Administration had identified as having died before 1974.

An examination of first hire dates into the Barrier Plant demonstrated that, of the 990 persons of interest, the greatest majority had been hired before 1954 (approximately 850 of the 990). Because the latency period between insult and clinical manifestation of disease is of particular interest in this study (estimated to be 20-30 years), it is recommended that the population for study should be limited to employees hired before 1954.

Statistical calculations were made using crude age adjustment methodologies to estimate the deaths which could be expected in this population, assuming that they had the same mortality experience as white males in the U. S. From these calculations, it was determined that we could expect 14.8 deaths due to all malignant disease, 4.3 deaths due to lung cancer, and 0.07 deaths due to malignancies of the nose, middle ear, and accessory sinuses.

Among the Barrier Plant workers hired before 1954, 85 are known to have died. Death certificates are available for 76 of them. Examination of these death certificates showed that 14 deaths were due to malignant disease, 2 of which were due to lung cancer, and none due to cancer of the nasal sinuses. Assuming that none of the 9 individuals for whom death certificates are not yet available have died of malignant disease, and that the expected deaths would not change significantly using different comparison groups and more careful age adjustments, there is no evidence at present that this population has an increased risk of lung cancer or cancer of the nasal sinuses. However, the size of the population is such that the observed number of cases is consistent with as much as a 50 percent increased incidence in lung cancer and a 4,000 percent increase in cancer of the nasal sinuses.

A carefully documented study of the mortality due to the two malignancies of interest can probably be completed within one year. However, it must be recognized that the population size is so limited that even if this population displays exactly the same mortality rates due to cancer of the lung and nasal sinuses as a similar population not exposed to nickel, these

findings would still be consistent with an increased risk of lung cancer and a large increased risk of nasal sinus malignancy. This statistical limitation of the population at risk, coupled with the fact that this population is just now coming into the assumed peak latency period, casts some doubt on the efficacy of using findings in this population to convince OSHA that the NIOSH recommendation for exposure limits of workers to elemental nickel powder is set too low.

OTHER HEALTH PROBLEMS - E. A. Tompkins & J. H. Godbold

A review of the death certificates thus far available for the test group suggests the possibility of other health problems beyond the two respiratory malignancies of specific interest in this project. If these suggested outcomes are indeed findings of the proposed epidemiologic investigation, further studies, specifically designed to evaluate these health problems, should be conducted.

ENVIRONMENTAL EXPOSURE - R. D. Gilmore

The air monitoring and personnel urinalysis data on computer printouts have been further studied. It is apparent that a full understanding of these historical data would be difficult to achieve. The bases for air monitoring values (whether routine or in response to exposure incidents), the specific locations or operations being monitored, the analytical methods and limits of detection - all may be important in understanding the data.

The urinalysis values for individual employees are also not readily interpretable. The past programs of monitoring, the limited amount of data per employee, the lack of values for many employees, the limitations and methods of laboratory analyses - all would be of concern in making use of these data in this study.

In general, the historical data on monitoring will, therefore, serve as supportive information for interpreting statistical judgments derived from detailed epidemiological study. The raw monitoring data, retrieved from storage in Plant Records vaults, may need close examination to gain best value from the CTC compilations.

At the present time, improved industrial hygiene practices are contributing more monitoring data regarding working environments. These new data continue to enter the computer banks and will support future studies.

PROJECT COMMUNICATIONS

A helpful compilation of facts and observations related to the ERDA Health and Mortality data files has been supplied by Mr. Howard L. Fore of the Computer Sciences Division. The information derived from his association with these data has been very useful and will undoubtedly become an important resource as this project continues.

Upper management of UCCND and ERDA-ORO, in two meetings conducted, respectively, on February 17 and 24, 1977, were informed of the progress in this project. Both of these meetings led to the following conclusions: (1) The epidemiologic study of workers exposed to nickel powder should be conducted, with a goal of having it in publishable form before the end of this calendar year. (2) As this investigation proceeds, if health effects other than malignancies of the respiratory system appear to be valid findings, specific parallel studies designed to evaluate these effects should be undertaken.

A meeting has been arranged for March 8, to inform members of INCO management of our present project status and the expected future work. INCO's interests and their role in sharing costs will also be discussed. This meeting will be attended by upper management of ERDA-ORO, K-25, and INCO.

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K/NI-1, Part 3

PROJECT PROGRESS REPORT FOR MARCH 1977
NIOSH STANDARDS EVALUATION OF NICKEL POWDER

C. W. Weber
Manager, NIOSH Standards Evaluation Project

J. C. White
UCCND Technical Services Manager

April 1, 1977

UNION CARBIDE

OAK RIDGE GASEOUS DIFFUSION PLANT
OAK RIDGE, TENNESSEE

prepared for the **U.S. ENERGY RESEARCH AND DEVELOPMENT ADMINISTRATION**
under **U.S. GOVERNMENT** *Contract W-7405 eng 26*

HIGHLIGHTS

In review discussions with management of UCCND, ERDA-ORO, and INCO, it was decided that a detailed epidemiologic study of K-25 Barrier Plant nickel workers should be started immediately.

In response to a letter of proposal from ORAU, specifying the scope and cost of a formal epidemiologic study of K-25 workers exposed to elemental nickel, a Memorandum Purchase Order was issued to ORAU to conduct the investigation.

The Computer Technology Center has begun work on identifying the possible controls for this study, in accord with specific criteria.

[redacted]

PROJECT PROGRESS REPORT FOR MARCH 1977
NIOSH STANDARDS EVALUATION OF NICKEL POWDER

INTRODUCTION

This project was organized to conduct an epidemiologic study of K-25 employees who have been occupationally exposed to elemental nickel powder, to evaluate whether such work leads to health problems, specifically increased incidence of respiratory malignant diseases. The study was proposed in December, 1976, following a review by ERDA-ORO, K-25, and the International Nickel Corporation (INCO) of a draft recommendation by the National Institute of Occupational Safety and Health (NIOSH) that the standard for airborne levels of nickel be reduced to 5 µg/cu m. Pure nickel was included in the recommendation, although no studies have been able to isolate exposure to elemental nickel from exposure to nickel compounds and impurities known to be associated with increased incidence of respiratory malignancies, particularly lung cancer and cancer of the nasal sinuses.

Because K-25 has used pure nickel in the manufacture of barrier for many years, this project can isolate the effects of exposure to nickel powder (elemental). A major resource for this project is the computerized information at the UCCND Computer Technology Center (CTC), collected for the ERDA Health and Mortality Study (H&MS). These data files include K-25 employee work histories and the dates of death for any employees known to have died before 1974.

Examination thus far of selected ERDA H&MS information indicated that a detailed epidemiology study of mortality due to lung and nasal sinus malignancies can be completed by the end of 1977. It was emphasized, however, that the small population of the subjects for the study will limit the statistical impact of the findings and also that this population is just now entering the assumed latency period (20-30 years) for the diseases of interest. In review discussions with management of UCCND, ERDA-ORO, and INCO, it was decided that the detailed study should begin immediately.

The formal detailed study is, therefore, under way, in the charge of Mrs. E. A. Tompkins, Epidemiologist, at ORAU (Oak Ridge Associated Universities). Support from members of K-25 will continue as needed, to provide information to Mrs. Tompkins and Dr. J. H. Godbold, Biostatistician.

[redacted]

PROJECT ORGANIZATION

Mr. S. S. Stief has been appointed to the project team. His past acquaintance with the project and its objectives, his familiarity with INCO's interests, his reliable attendance at major meetings, and his direct association with plant management are all assets to the work of the group.

EPIDEMIOLOGIC STUDY - E. A. Tompkins & J. H. Godbold

The preliminary survey of K-25 nickel workers who had been employed in the Barrier Plant indicated a total of about 990 through the year 1973. Of these, approximately 850 were hired before 1954. Because the latency period for respiratory malignancies is an important consideration, it was recommended that the population for study be limited to employees hired before 1954.

After considering the various ways of selecting a control population with which to compare the population of exposed nickel workers, it was decided to choose a random sample of white males initially hired at K-25 prior to January 1, 1954. Since no cases of lung cancer have occurred in white females or in non-whites in the exposed population, such individuals cannot be used in analysis. The CTC has begun work on identifying possible controls. The total list will exclude any employees who worked in the Barrier Plant, any who had known or potential exposure to nickel or its compounds, and welders. The sampling of the control population will be completed after it is known how many potential controls are available.

Arrangements are being made to transfer certain computer programs and vital statistics data from the computer group at ORNL to CTC. These programs will be used in the analysis of data to compute person-years-at-risk and also the expected number of deaths due to specific causes in this study.

EMPLOYEE SMOKING HABITS - T. G. Fortney & E. A. Tompkins

In an epidemiologic study with emphasis on respiratory disease, the smoking habits of the subjects and the control group may be important. Fortunately, the Medical Records of most employees contain some entries on the smoking habits of workers at K-25 at the time they were hired. These data will be

used as an indicator of smoking history. Arrangements are being made to retrieve this information in a systematic approved manner. For the employees involved, both subjects and controls, it is anticipated that about 85% of their medical records have been placed in the Plant Records vault following termination.

OCCUPATIONAL EXPOSURE DATA - R. D. Gilmore

During this reporting period, no significant progress was made in the evaluation of historical air monitoring and personnel urinalysis data pertaining to nickel. Industrial Hygiene field monitoring records for the years 1944 through 1962 have been retrieved from the Plant Records storage vault and will be used to supplement data available on computer printouts. Occupational exposure data will be of more significance in the later phases of this study, as support for interpretation of findings. The Industrial Hygiene Department plans to assign a high priority to this project during May and June, 1977, to assure that the data are evaluated and summarized by August 1, 1977.

PROJECT COMMUNICATIONS

An information meeting was held on March 8, 1977, to inform visiting members of INCO management of our project status and expected future work. The INCO representatives were pleased with the work done to date and stated their desire to share the costs of the nickel study, through a written agreement. The INCO representatives also stated that they would probably be interested in support of animal studies involving nickel exposure. K-25 management agreed to pursue this interest for INCO, probably at ORNL; if such a project were initiated, it is intended to be apart from this epidemiology study in both pursuit and support.

A thorough review was made to establish the payroll accounts to which Barrier Plant workers have been assigned since the beginning of that manufacturing activity at K-25. Through discussions with personnel of the K-25 Accounting and Budget Office, the Computer Sciences Division, and Plant Records, it was concluded that only two payroll accounts are involved in identifying the Barrier Plant nickel workers from the beginning of operations until 1954. Other identified operating accounts, which closed to these two payroll accounts, will probably associate the past Industrial Hygiene monitoring programs with that area.

Because K-25 is a uranium processing plant and had received uranium trioxide for the Feed Plant operations for many years, the question of lung exposure to radon-daughter products (from radium contamination) was raised by Mrs. Tompkins. There is no indication that radon-exhalation tests have been conducted on any K-25 employees; also evidently no analyses of UO_3 were made for radium. Presumably the purity requirements for the UO_3 would have demanded chemical separations which excluded radium. This very pertinent question may need further attention.

COORDINATION AND CONTROL

A letter of proposal was received from ORAU (Oak Ridge Associated Universities) specifying the scope and cost of the formal epidemiology study of Barrier Plant nickel workers. Following prompt agreement by K-25 management, a Memorandum Purchase Order was sent to ORAU covering the funding authorization.

A formal agreement with INCO has not yet been executed, regarding their proposal to share the costs of this study.

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PROJECT PROGRESS REPORT FOR APRIL 1977
NIOSH STANDARDS EVALUATION OF NICKEL POWDER

C. W. Weber
Manager, NIOSH Standards Evaluation Project

J. C. White
UCCND Technical Services Manager

May 1, 1977

UNION CARBIDE

OAK RIDGE GASEOUS DIFFUSION PLANT
OAK RIDGE, TENNESSEE

prepared for the **U.S. ENERGY RESEARCH AND DEVELOPMENT ADMINISTRATION**
under **U.S. GOVERNMENT** *Contract W-7405 eng 26*

HIGHLIGHTS

The epidemiologic study is awaiting final selection of the employee control group, from a list of possible controls supplied by the Computer Technology Center.

A proposed contract has been sent to INCO for their consideration.

PROJECT PROGRESS REPORT FOR APRIL 1977
NIOSH STANDARDS EVALUATION OF NICKEL POWDER

INTRODUCTION

The epidemiologic study of K-25 employees who have been occupationally exposed to elemental nickel powder is underway. The major source of information for the project is the computerized data on employee work histories and dates of death, collected for the ERDA Health and Mortality Study.

The Computer Technology Center, which handles this data bank, has recently compiled a listing of possible control employees for this study. This was sent to Mrs. E. A. Tompkins, Epidemiologist, at ORAU (Oak Ridge Associated Universities) for review and further instructions for final selection of controls.

After receiving final listings of both the subjects and controls for the study, the work will become more methodical.

EPIDEMIOLOGIC STUDY - E. A. Tompkins & J. H. Godbold

No reportable progress on this study has been made this month. The Computer Technology Center furnished, late in April, a printout of ORGDP employees identified as possible controls for the study. This is presently being reviewed before the actual selection of controls will be made.

EMPLOYEE SMOKING HABITS - T. G. Fortney & E. A. Tompkins

The retrieval of certain relevant information on the smoking habits of employees, to be accomplished by examination of medical records, has not begun. This phase of work also awaits the final determination of control employees.

CONTRACT WITH INCO - S. S. Stief

International Nickel, Inc. (INCO) has agreed to share the costs of this study. A proposed contract has been formulated and approved by ERDA-ORO. It has been sent to INCO for their consideration, but was not yet approved at the end of April.

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PROJECT PROGRESS REPORT FOR MAY 1977
NIOSH STANDARDS EVALUATION OF NICKEL POWDER

C. W. Weber
Manager, NIOSH Standards Evaluation Project

J. C. White
UCCND Technical Services Manager

June 1, 1977

UNION CARBIDE

OAK RIDGE GASEOUS DIFFUSION PLANT
OAK RIDGE, TENNESSEE

prepared for the **U.S. ENERGY RESEARCH AND DEVELOPMENT ADMINISTRATION**
under **U.S. GOVERNMENT** *Contract W-7405 eng 26*

HIGHLIGHTS

NIOSH has formally recommended to OSHA that the exposure limit for inorganic nickel (including elemental nickel) be set at 15 µg/cu m.

The epidemiologic study awaits final listings from CTC of the subject and control groups of K-25 employees.

ERDA-ORO and INCO have executed a contract through which INCO will bear 50% of the costs of the epidemiologic study.

PROJECT PROGRESS REPORT FOR MAY 1977
NIOSH STANDARDS EVALUATION OF NICKEL POWDER

INTRODUCTION

An epidemiologic study of K-25 employees who have been occupationally exposed to elemental nickel powder is being conducted. Mortality due to respiratory malignancies is the emphasis of the study. Such research was recommended by the National Institute of Occupational Safety and Health (NIOSH), since no equivalent investigation has been done.

On May 13, 1977, NIOSH recommended to the Occupational Safety and Health Administration (OSHA) that an exposure limit for inorganic nickel be set at 15 µg/cu m of air. (For most industrial laboratories, this is considered to be the lowest detectable level of nickel.) In lieu of data which isolate exposure to elemental nickel from exposure to nickel compounds and impurities known to be health problems, pure nickel is included in that recommendation.

OSHA must decide whether to tighten its nickel standard to the 15 µg/cu m level and whether to include elemental nickel in the standard. The ongoing epidemiologic study of K-25 employees, scheduled for completion by the end of this year, may assist in that evaluation.

EPIDEMIOLOGIC STUDY - E. A. Tompkins and J. H. Godbold

The Computer Technology Center (CTC) furnished a listing of K-25 employees who are candidates for controls. Following review of this list, it was decided to limit the controls to those white males who were hired initially before January 1, 1954, but did not terminate before January 1, 1948. The control list will exclude white females and nonwhite employees, since preliminary study indicated no cases of lung cancer occurring among such individuals in the exposed population, and will exclude all Barrier Plant employees or those who had known or potential occupational exposure to nickel.

The CTC has been given instructions on how to select the sample of controls from the population defined above. Further analytical work awaits the final listings of controls and subjects for the study.

CONTRACT WITH INCO - S. S. Stief

In early May a contract was approved by both ERDA-ORO and International Nickel (U.S.), Inc. (INCO). As agreed in prior discussions, INCO will bear 50% of the ERDA fund costs of the epidemiologic study of elemental nickel.

COORDINATION AND CONTROL

An additional special account has been set up to collect one-half of all costs associated with the study. On a fiscal quarterly basis, UCCND will invoice INCO for all costs collected in the new account. The first such invoice will be issued at the end of June 1977.

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PROJECT PROGRESS REPORT FOR JUNE 1977
NIOSH STANDARDS EVALUATION OF NICKEL POWDER

C. W. Weber
Manager, NIOSH Standards Evaluation Project

J. C. White
UCCND Technical Services Manager

July 1, 1977

UNION CARBIDE

OAK RIDGE GASEOUS DIFFUSION PLANT
OAK RIDGE, TENNESSEE

prepared for the **U.S. ENERGY RESEARCH AND DEVELOPMENT ADMINISTRATION**
under **U.S. GOVERNMENT** *Contract W-7405 eng 26*

HIGHLIGHTS

Current efforts emphasize the formalization of a valid and representative list of control employees for use in the epidemiologic study.

Applicable information on individual smoking habits will not be available from medical records of subject and control employees, because the information did not enter the records until appreciably after the employment period of interest in this study.

Occupational exposure to elemental nickel in the barrier plant since 1948 is being investigated through the Industrial Hygiene monitoring records.

PROJECT PROGRESS REPORT FOR JUNE 1977
NIOSH STANDARDS EVALUATION OF NICKEL POWDER

INTRODUCTION

An epidemiologic study of K-25 employees who have been occupationally exposed to elemental nickel powder is being conducted. Mortality due to respiratory malignancies is the emphasis of the study. Such research was recommended by the National Institute of Occupational Safety and Health, since no equivalent investigation has been done.

Controls for the study will be K-25 employees who have not been exposed to nickel but who were employed during the same time period as the subject nickel workers. Much of the recent effort has involved computer programming and printouts by L. F. Denton and H. L. Fore of the Computer Technology Center (CTC) to assist the epidemiologist, Mrs. E. A. Tompkins, and biostatistician, J. H. Godbold (ORAU), in formalizing the lists of employees.

About 2400 employees (both subjects and controls) will be used in the study. The work histories of these employees are available from the CTC in the compilation of the ERDA Health and Mortality Study (H&MS) data.

The project is advancing at a reasonable pace, with its completion scheduled for the end of this year. The findings in this epidemiologic study may be helpful to the Occupational Safety and Health Administration (OSHA), in its evaluation of required standards for exposure to elemental nickel.

EPIDEMIOLOGIC STUDY - E. A. Tompkins and J. H. Godbold

The set of potential control employees was reviewed and, in accord with instructions to CTC, a subset was generated for use in the epidemiologic study. Identified as K-25 employees who were on the payroll between January 1, 1948, and January 1, 1954, (and meeting other criteria) the initial set of about 6500 employees was reduced to a subset of about 1600.

A printout of the reduced list is being examined to assure that it is a representative sample of the larger non-nickel population.

EMPLOYEE SMOKING HABITS - T. G. Fortney and C. W. Weber

It is apparent that no applicable information on the smoking habits of employees can be derived from their individual medical records. It was hoped that such information would be available from an entry on the Cornell Medical Index Health Questionnaire. Unfortunately, the use of this employee questionnaire was not started until 1955, so the period of employment relevant to this study would predate its use.

OCCUPATIONAL EXPOSURE DATA - R. D. Gilmore

All nickel urinalysis data available for the selected study population have been collected. These data are being reviewed to determine their potential significance to this study. Industrial Hygiene field monitoring records for the period since 1944 were also collected and are being reviewed to compile the available air monitoring data which relate to the nickel study population.

The Industrial Hygiene Department has assigned a staff member to coordinate this review to assure that the available data are evaluated and summarized in a timely manner.

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PROJECT PROGRESS REPORT FOR JULY 1977
NIOSH STANDARDS EVALUATION OF NICKEL POWDER

C. W. Weber
Manager, NIOSH Standards Evaluation Project

J. C. White
UCCND Technical Services Manager

August 1, 1977

UNION CARBIDE

OAK RIDGE GASEOUS DIFFUSION PLANT
OAK RIDGE, TENNESSEE

prepared for the **U.S. ENERGY RESEARCH AND DEVELOPMENT ADMINISTRATION**
under **U.S. GOVERNMENT** *Contract W-7405 eng 26*

HIGHLIGHTS

The cooperation of many supporting organizations, both within and outside of K-25, is keeping this project on a reasonable schedule.

The list of controls was finalized; therefore, work is underway on the tabulation of causes of death among that group. The search has also begun for missing death certificates for deaths among the nickel subjects and control employees.

Information on employee smoking habits is being retrieved from medical records for both nickel workers and controls, even though the data entered the records after the employment period of specific interest.

PROJECT PROGRESS REPORT FOR JULY 1977
NIOSH STANDARDS EVALUATION OF NICKEL POWDER

INTRODUCTION

An epidemiologic study of K-25 employees who have been occupationally exposed to elemental nickel powder is being conducted. The National Institute of Occupation Safety and Health (NIOSH) has recommended such research, because no previous investigations have suitably isolated exposure to elemental nickel from exposure to nickel compounds and/or impurities known to be hazards to health. The emphasis in the study is mortality due to respiratory malignancies. In the recent NIOSH recommendations for workplace exposure to inorganic nickel, respiratory protection is especially emphasized and a maximum tolerable nickel concentration of 15 µg/cu m, as a time-weighted average for up to a 10-hour work shift, is proposed.

The epidemiologic study of K-25 nickel workers is progressing well. The cooperation of many supporting organizations has become important to the project. Notable among recent support efforts have been the programming and printouts by the Computer Technology Center (CTC), computer tapes of vital statistics from the Computer Science Division at the Oak Ridge National Laboratory (ORNL), and the coordinated help of the Plant Records staff in supplying information to the Medical and Industrial Hygiene Departments.

The project is being paced toward a completion report draft in October. The findings of the epidemiologic study may be helpful to the Occupational Safety and Health Administration (OSHA) in its evaluation of required standards for exposure to elemental nickel.

EPIDEMIOLOGIC STUDY - E. A. Tompkins and J. H. Godbold

A finalized list of 1637 controls was established by CTC and sent to the epidemiologist. This list is a 25 percent sample of all employees (excluding those with potential exposure to nickel, and meeting certain other criteria) who were on the K-25 payroll between January 1, 1948, and January 1, 1954. Of these controls, death certificates are lacking for 19 of the deaths. A national search will now be made among the state departments of vital statistics for these death certificates, as well as for the three missing death certificates for deaths in the exposed nickel population.

Work has begun on the compilation of causes of death among the control group, for comparison with the incomplete data from the nickel subject group.

Arrangements are currently being made to acquire the computer tapes containing U. S. vital statistics data necessary for the calculation of expectancies of mortality. Some of these tapes are already available at ORNL, through the cooperation of A. S. Loebl and J. F. Hull, while others may have to be prepared at the CTC from base vital statistics data. Inquiries are being made to the National Center for Health Statistics for computer tapes of mortality data for the appropriate years.

EMPLOYEE SMOKING HABITS - T. G. Fortney, A. Estes, and C. W. Weber

It had been noted that the Cornell Medical Index Health Questionnaire, completed by employees for their medical records, was not in use at K-25 until 1955; the employment period of interest in this study, therefore, predates its use. It was decided, however, to gather the earliest data available on the smoking habits of both the nickel subjects and the controls, appropriately qualifying the information. Most of the employees in both groups were still on the payroll in 1955.

It will be assumed that any bias in the smoking statistics, as a result of changes in personnel habits, will be approximately equal in both groups, so that some valid comparisons can be made.

The retrieval of information from medical records involves examining files presently in the K-25 Medical Department and gathering data from Plant Records vaults. This effort has been greatly implemented through computer printouts which appropriately combine each employee's identity with his termination date, medical number, and badge number. The assistance of C. J. Parrish and E. B. Williams of Plant Records in the retrieval of medical records has been extremely helpful in this phase of study.

OCCUPATIONAL EXPOSURE DATA - R. D. Gilmore

During the month of July, the air monitoring data for nickel in the Barrier Plant during the period 1954 to 1964 were compiled from Plant Records. No nickel data were found for earlier years. The collected data were categorized by sample location and date, in an effort to characterize the various

processes involving a potential exposure to elemental nickel. The data are currently being evaluated by the K-25 Industrial Hygiene Department to identify trends, significant changes in potential exposures, "normal" concentrations and ranges. Work is progressing satisfactorily and the data will be forwarded to the project epidemiologist and biostatistician for review in the near future.

PROJECT COMMUNICATIONS - S. S. Stief

Arrangements were made for a meeting in Oak Ridge with several members of management at INCO (United States), Inc., and its subsidiary, Huntington Alloys, Inc. In addition to updating the management of INCO, ERDA, and UCCND on the epidemiology project, other interests to be discussed are: the efforts by OSHA to establish nickel standards; possible ORNL participation in animal inhalation studies with nickel and selected compounds; and a review of the work environment measurements of airborne nickel powder.

The meeting was scheduled for August 2, 1977, at the Federal Office Building.

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K/NI-1, Part 8

PROJECT PROGRESS REPORT FOR AUGUST 1977 NIOSH STANDARDS EVALUATION OF NICKEL POWDER

C. W. Weber
Manager, NIOSH Standards Evaluation Project

J. C. White
UCCND Technical Services Manager

September 1, 1977

UNION CARBIDE

OAK RIDGE GASEOUS DIFFUSION PLANT
OAK RIDGE, TENNESSEE

prepared for the **U.S. ENERGY RESEARCH AND DEVELOPMENT ADMINISTRATION**
under **U.S. GOVERNMENT** *Contract W-7405 eng 26*

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HIGHLIGHTS

The epidemiologic study is progressing steadily although certain critical information has not yet been received. (Page 3)

The search of medical records for employee smoking habits has now reached into the other UCCND plants to cover transferees from K-25. (Page 4)

Air monitoring data for nickel in the Barrier Plant have been compiled for the period from 1948 through 1963. (Page 5)

A meeting was held with INCO representatives on August 2, 1977, to discuss several topics of mutual interest regarding nickel. (Page 5)

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PROJECT PROGRESS REPORT FOR AUGUST 1977
NIOSH STANDARDS EVALUATION OF NICKEL POWDER

INTRODUCTION

The epidemiologic study of K-25 employees who have been occupationally exposed to elemental nickel powder is continuing. The National Institute of Occupational Safety and Health (NIOSH) has recommended such research, because previous investigations have not suitably isolated exposure to elemental nickel from exposure to nickel compounds and/or impurities known to be hazards to health.

The study is quickening its pace somewhat, as more information is becoming available. At the same time, the urgency for completing certain phases has increased. A high level of cooperation by supporting organizations, now including the medical departments at other UCCND plants, has helped in the gathering of facts and treatment of data. However, the project still awaits certain critical information, including missing death certificates.

A completion report draft is anticipated in October, for review by UCCND, ERDA, and INCO. The findings of the epidemiologic study may be helpful to the Occupational Safety and Health Administration (OSHA) in its consideration of workplace standards for elemental nickel exposure.

EPIDEMIOLOGIC STUDY - E. A. Tompkins and J. H. Godbold

A list of deceased persons has been submitted to the departments of vital statistics of all 50 states in a search for death certificates still not obtained. This search covers missing certificates for 3 exposed nickel workers and 19 controls. Among the causes of death tabulated from certificates obtained to-date, no cases of nasal sinus cancer were found. However, a variety of malignancies were noted, as expected, in both groups.

A purchase order was issued to the National Center for Health Statistics for microfiche copies of United States population death data which will be used to calculate the expected number of deaths in our two study groups (nickel workers and controls). These data have not yet arrived.

The Computer Technology Center (CTC) has received computer tapes of national population and mortality statistics for the years 1950-1970, presented in five-year age groups and tabulated by sex and race. These tapes, supplied by the Computer Science Division at ORNL, will permit calculation of some of the death expectancy figures.

Analysis is underway on the distribution by year of initial hire and age at initial hire in the two study groups. Also, we are in the process of analyzing the socioeconomic status (principally using payroll indicators) of the employees in the two groups as a function of the length of employment.

EMPLOYEE SMOKING HABITS - T. G. Fortney, A. Estes, and C. W. Weber

The search of medical records to identify smoking habits of individual employees has progressed well for those records expected to be at K-25; about 70 records have not yet been found. A larger group (about 185) represent people who have transferred to Y-12, ORNL, or the Paducah Gaseous Diffusion Plant. We are actively engaged with the medical departments at those plants in finding records and retrieving data.

Of about 2,420 medical records involved, approximately 1,070 contained no questionnaire from which to identify smoking habits. The effects of smoking among both the subject and the control groups will, therefore, involve the data from about 1,350 records, of which 250 are still being sought.

SEARCH OF EMPLOYEE RECORDS - A. Estes and C. W. Weber

In addition to individual smoking habits, the medical records have provided information to confirm other personnel data. The computerized information on employees, stored in the data banks for the ERDA Health & Mortality Study (H&MS) at the CTC, contains some errors (a small fraction of the thousands of facts) which should be corrected, if possible. A number of corrections have already been made, relevant to the employees in the two study groups.

Several errors in employee sex or race have been found while using the medical records to confirm those particulars. Other errors were found in social security numbers, and employees' names and initials. Because the computer printouts generally provide facts no more recent than 1974, a considerable number of data omissions, especially termination dates, have been identified in the work with medical records.

Other records, if available, may need to be searched to authenticate some personnel information. In some cases, where the medical records are still missing, even sex and race confirmation is incomplete and may require access to personnel records. Inconsistent data on dates of birth and dates of hire need to be resolved. A number of questions about work history, especially dates of entry to certain department payrolls, remain unanswered. These problems are being pursued systematically and through the appropriate lines of management.

OCCUPATIONAL EXPOSURE DATA - R. D. Gilmore

The air monitoring data for nickel in the Barrier Plant were compiled for the period from 1948 through 1963. The tabulated values represent more than 3,000 samples collected over that period; the averages and ranges of values, with some statistical treatment, are compiled by year and by work area (operation) in the Barrier Plant. The information will soon be forwarded to the epidemiologist.

PROJECT COMMUNICATIONS - S. S. Stief

A meeting was held with representatives of the International Nickel Company at the Federal Office Building in Oak Ridge on August 2, 1977, to discuss the following topics: the status of proposed new OSHA standards for airborne nickel in work environments; the progress of the epidemiologic study of nickel workers at K-25; the air monitoring measurements of nickel in the Barrier Plant; and the possibility of ORNL participation in animal inhalation studies with nickel and selected compounds.

The meeting was a successful exchange of information. Dr. J. B. Storer, who outlined a suggested program for animal studies in the ORNL Biology Division, has submitted a detailed proposal, prepared promptly after the meeting. That proposal is now being reviewed at K-25.

It was also agreed at the August 2 meeting that K-25 would provide INCO with any information developed here about the thickness of an oxide film on nickel particles exposed to air.

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K/NI-1, Part 9

PROJECT PROGRESS REPORT FOR SEPTEMBER 1977
NIOSH STANDARDS EVALUATION OF NICKEL POWDER

C. W. Weber
Manager, NIOSH Standards Evaluation Project

J. C. White
UCCND Technical Services Manager

October 1, 1977

UNION CARBIDE

OAK RIDGE GASEOUS DIFFUSION PLANT
OAK RIDGE, TENNESSEE

prepared for the **U.S. ENERGY RESEARCH AND DEVELOPMENT ADMINISTRATION**
under **U.S. GOVERNMENT** *Contract W-7405 eng 26*

HIGHLIGHTS

Critical United States mortality data have been received from the National Center for Health Statistics, permitting keypunch, computer program, and computational work. (Page 4)

The search of employee records for individual smoking habits and other information is nearly complete. (Page 4)

Occupational nickel exposure data from historical records have been compiled and organized for use by the epidemiologist. (Page 5)

PROJECT PROGRESS REPORT FOR SEPTEMBER 1977
NIOSH STANDARDS EVALUATION OF NICKEL POWDER

INTRODUCTION

The epidemiologic study of K-25 employees who have been occupationally exposed to elemental nickel powder has progressed well. The National Institute of Occupational Safety and Health (NIOSH) recommended such research, since no equivalent investigation has been done. The Occupational Safety and Health Administration (OSHA) received the NIOSH recommendations for a reduced exposure limit for inorganic nickel in May, 1977. OSHA then published in the September 27, 1977 Federal Register a request for information on inorganic nickel, including occupational exposure; a deadline of November 1, 1977 was announced for submitting information.

This project is approaching the advanced stages of analytical work. All essential information has been obtained except 22 death certificates from the state departments of vital statistics. Computer calculation of United States mortality expectancies will soon be completed for comparison with empirical values in the nickel subject and control groups.

PROJECT COSTS

During the month of September, the project costs through August were computed, as presented below:

	Expenditure	Budget	Percent Expended
Management & Staff	$ 37,100	$ 58,300	64
Oak Ridge Assoc. Univ.	29,244	50,000	58
Computer & Other Expense	9,577	27,700	35
	36,714	64,000	57
TOTAL	$112,635	$200,000	56

EPIDEMIOLOGIC STUDY - E. A. Tompkins and J. H. Godbold

The analysis of work histories of nickel workers and controls is continuing, with payroll status versus length of employment being examined as an indicator of socioeconomic status. We have also begun recoding the causes of death on the death certificates to reflect the numerical coding appropriate to the year of death.

We have received United States mortality data for the appropriate years, from the National Center for Health Statistics. Although it was hoped to receive these data in the form of computer tapes, or microfiche, which could permit ready keypunching, the material arrived on microfilm cassettes. These have been used to supply hard copy (photocopy) for illegible or missing material among statistical tables previously in hand.

Prior to receipt of the microfilm data, a computer printout and program were obtained from the Biostatistics Department at Harvard University, which could be used to compute United States mortality expectancies. Fortunately, the health statistics from the National Center arrived before significant effort was expended with the more time-consuming and tedious application of the Harvard program.

Keypunching arrangements are being made to employ the National Center statistics for the scope of diseases and years pertinent to this study. We continue to make corrections in the data for the subject and control employees, as information is retrieved from medical and personnel files. We are still waiting for the 22 outstanding death certificates from the state departments of vital statistics.

SEARCH OF EMPLOYEE RECORDS - T. G. Fortney, A. Estes, and C. W. Weber

The search of medical records to identify smoking habits of individual subject and control employees has been very successful, at K-25 as well as the other three UCCND plants. The records of more than 200 employees who had transferred to Y-12, ORNL, or the Paducah Gaseous Diffusion Plant were retrieved in this search.

Forty-four medical records have not been found for employees who terminated from K-25. The reasons for these missing records are not known. Of about 1350 medical records expected to contain relevant smoking data, the 44 missing records represent about 3%; for purposes of this study, this loss is not significant. No remaining approach to finding these records is apparent, except a complete Plant Records vault search, which is presently unreasonable.

Personnel records have also proved extremely helpful in confirming sex and race of employees and in finding information on dates of birth, hire, termination, transfer, and other matters of work history.

OCCUPATIONAL EXPOSURE DATA - R. D. Gilmore

The air monitoring data for nickel in the Barrier Plant were organized and compiled for the period from the beginning of operation in 1948 through 1963. From 1964 to 1973, the last year pertinent to this study, practically no data were collected. The monitoring values are compiled by year and area of operation in the Barrier Plant. All results are now ready to forward to the epidemiologist.

Urinalysis data for the period from 1948 through 1973 are being reviewed for possible applicability to the study. However, these individual personnel values are not generally interpretable in terms of exposure levels.

PROJECT COMMUNICATIONS - S. S. Stief and C. W. Weber

The project-related proposal by Dr. J. B. Storer, ORNL Biology Division, for animal inhalation studies with nickel and nickel oxide powders was reviewed by UCCND management and recommended to DOE-ORO. It has not yet been approved.

At the August meeting with INCO, we agreed to share any information developed at K-25 about the thickness of an oxide film on nickel particles. This interest led to a brief study, soon to be reported by development personnel and transmitted to INCO.

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K/NI-1, Part 10

PROJECT PROGRESS REPORT FOR OCTOBER 1977
NIOSH STANDARDS EVALUATION OF NICKEL POWDER

C. W. Weber
Manager, NIOSH Standards Evaluation Project

J. C. White
UCCND Technical Services Manager

November 1, 1977

UNION CARBIDE
OAK RIDGE GASEOUS DIFFUSION PLANT
OAK RIDGE, TENNESSEE

[redacted]

prepared for the **U.S. DEPARTMENT OF ENERGY** *under*
U.S. GOVERNMENT *Contract W-7405 eng 26*

HIGHLIGHTS

Advanced computational work has begun at ORAU using the U.S. mortality expectancies and the empirical statistics from the subject and control groups of the epidemiologic study.

All smoking history information on individual subject and control employees has been compiled and submitted to the epidemiologist and biostatistician.

All relevant available historical records of occupational exposure to nickel in the K-25 Barrier Plant were summarized by year and work area and submitted to the epidemiologist.

PROJECT PROGRESS REPORT FOR OCTOBER 1977
NIOSH STANDARDS EVALUATION OF NICKEL POWDER

INTRODUCTION

The epidemiologic study of K-25 employees who have been occupationally exposed to elemental nickel powder is in its advanced stages of analytical work. The mortality data for the full period from 1948 through 1973 were received from the National Center for Health Statistics. The keypunched data tape of the relevant facts was supplied by the K-25 Computer Technology Center (CTC) to the Oak Ridge Associated Universities (ORAU) Computer Center for use in the program developed by ORAU.

A letter was forwarded to the Department of Energy - Oak Ridge Operations regarding a request by the Occupational Safety and Health Administration (OSHA) for information on occupational exposure to inorganic nickel. The OSHA request appeared in the September 27, 1977 Federal Register. Our letter points out that this formal study is underway, and a report is expected to be available early in CY 1978.

PROJECT COSTS

During the month of October, the project costs through September were computed, as presented below:

	Expenditure	Budget	Percent Expended
Management & Staff	$ 37,100	$ 58,300	64
Oak Ridge Assoc. Univ.	43,056	50,000	86
Computer & Other	10,946	27,700	40
Expense	42,655	64,000	67
TOTAL	$133,757	$200,000	67

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EPIDEMIOLOGIC STUDY - E. A. Tompkins and J. H. Godbold

During October, we received additional data from the National Center for Health Statistics. This completed the material needed on mortalities from a wide range of diseases for the years included in the study; data for 1973 had not been included in the earlier shipment. All relevant data were appropriately identified and keypunched on tape for computer use. This information will provide the mortality expectancy figures necessary for statistical treatment of the nickel and control groups in this study. Arrangements have been made with the K-25 CTC and the Computer Center at ORAU for the transfer of key-punched data to ORAU for computation in the person-years program which ORAU has already developed.

The information which has been collected on employee smoking habits is being tabulated and formalized suitably for presentation and interpretation. Death certificates are being received from various state departments of vital statistics on those deceased members of our study population for whom we previously had no death certificates.

SEARCH OF EMPLOYEE RECORDS - T. G. Fortney, A. Estes, and C. W. Weber

The search of medical records to identify smoking habits of individual members of the subject and control groups is complete. All gathered information was entered onto computer printout tables and submitted to the epidemiologist and biostatistician. Smoking histories were obtained from health questionnaires which had been filled out by the employees. Of about 2,400 employees in the study, about 1,300 provided relevant smoking data; information was lacking for the rest, primarily because they were terminated prior to 1955, when the questionnaires came into use at K-25.

A variety of revisions and additions have been made to the computerized employee information provided from the Health and Mortality Study (H&MS) bank of facts at the CTC. For the subject and control employees used in this study, revisions made as a result of searching basic records are being entered onto a spare printout list, to provide CTC personnel a basis for correcting their computer tapes for future use.

OCCUPATIONAL EXPOSURE DATA - R. D. Gilmore

The K-25 Industrial Hygiene Department completed its review of available plant records that could potentially provide data descriptive of occupational exposures to nickel in the barrier manufacturing facilities. With emphasis on the period from 1948 to 1973, no retrievable useful data were found for the years 1964 to 1973.

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For the years 1948 to 1963, all useful air monitoring data were organized by year and Barrier Plant work area. With more than 3,000 samples identified, the exposure data were tabulated with mean values, standard deviations, concentration ranges, and other summarized facts. The final compilation of information has been submitted to the epidemiologist.

Biological monitoring (urinalysis) records were also reviewed, but judged to be inadequate for use as indicators of occupational exposure to nickel at this time.

PROJECT COMMUNICATIONS - S. S. Stief and C. W. Weber

The project-related proposal by Dr. J. B. Storer, ORNL Biology Division, for animal inhalation studies with nickel and nickel oxide powders is under consideration by DOE-ORO and INCO.

Information developed at K-25 on the thickness of oxide film on nickel particles has been reviewed. This information will soon be transmitted to INCO in accord with our agreement in the August meeting with INCO management.

A letter was sent to DOE-ORO regarding the OSHA request for information on occupational exposure to inorganic nickel. The advanced status of this epidemiology study was indicated.

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PROJECT PROGRESS REPORT FOR NOVEMBER 1977 NIOSH STANDARDS EVALUATION OF NICKEL POWDER

C. W. Weber
Manager, NIOSH Standards Evaluation Project

J. C. White
UCCND Technical Services Manager

December 1, 1977

UNION CARBIDE

OAK RIDGE GASEOUS DIFFUSION PLANT
OAK RIDGE, TENNESSEE

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prepared for the **U.S. DEPARTMENT OF ENERGY** *under*
U.S. GOVERNMENT *Contract W-7405 eng 26*

HIGHLIGHTS

The completion report draft for the epidemiologic findings is being reviewed and will soon be submitted to management of UCCND, DOE-ORO, and INCO for comment.

The Occupational Safety and Health Administration (OSHA) has been formally advised of the advanced status of this study.

PROJECT PROGRESS REPORT FOR NOVEMBER 1977
NIOSH STANDARDS EVALUATION OF NICKEL POWDER

INTRODUCTION

The epidemiologic study of K-25 employees who have been occupationally exposed to elemental nickel powder is almost complete. All of the critical information needed has been received except a few death certificates. The final report of the findings has been drafted and is under preliminary review. It will soon be completed and submitted to UCCND, DOE-ORO, and INCO for comment.

A document was submitted to the Department of Labor - OSHA by DOE-ORO in response to the September 27, 1977 Federal Register request by OSHA for information on occupational exposure to inorganic nickel. Prepared at K-25, the document comments on the proposed reduction in exposure standards and also indicates that a report of this epidemiologic study is expected to be available early in 1978.

PROJECT COSTS

During the month of November, the project costs through October were computed, as presented below:

	Expenditure	Budget	Percent Expended
Management & Staff	$ 37,100	$ 58,300	64
Oak Ridge Assoc. Univ.	43,052	50,000	86
Computer & Other Expense	12,626 43,285	27,700 64,000	46 68
TOTAL	$136,063	$200,000	68

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EPIDEMIOLOGIC STUDY - E. A. Tompkins and J. H. Godbold

A report draft of the epidemiologic findings of this study was submitted to the project manager and committee for preliminary review. Revisions and graphic arts work will be completed before submitting the report to the management of UCCND, DOE-ORO, and INCO for final review. To eliminate problems of eventual journal publication, this report will probably be issued as an unclassified K-report, in which the body of the report will be the epidemiologic findings by ORAU. In that form, the report will be available to OSHA during their consideration of standards for nickel exposure.

All of the death certificates for the nickel worker group have been received except for one death, which occurred in Viet Nam. The remaining missing certificates are for 12 control employees, 1 of whom died in a foreign country. Only 9 of the 50 states have not responded to date, in the search for missing death certificates.

Receipt of the remaining death certificates will probably change some of the present statistics. However, no significant revisions are expected in the findings or the conclusions of this study.

PROJECT COMMUNICATIONS - S. S. Stief and C. W. Weber

The project-related proposal by Dr. J. B. Storer, ORNL Biology Division, for animal inhalation studies with nickel and nickel oxide powders has been reviewed by INCO. That company has returned a suggested revised program, more comprehensive in scope and more expensive than the original proposal. This revised plan is now being considered by UCCND and DOE-ORO.

Information developed at K-25 on the thickness of oxide film on nickel particles has been sent to INCO. This was a subject of inquiry in the August meeting with INCO management.

A document prepared at K-25 was sent to the Department of Labor - OSHA by DOE-ORO in response to the OSHA request for information on occupational exposure to inorganic nickel. The advanced status of this epidemiology study was indicated.

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PROJECT PROGRESS REPORT FOR DECEMBER 1977 NIOSH STANDARDS EVALUATION OF NICKEL POWDER

C. W. Weber
Manager, NIOSH Standards Evaluation Project

J. C. White
UCCND Technical Services Manager

January 20, 1978

UNION CARBIDE
OAK RIDGE GASEOUS DIFFUSION PLANT
OAK RIDGE, TENNESSEE

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prepared for the **U.S. DEPARTMENT OF ENERGY** *under*
U.S. GOVERNMENT *Contract W-7405 eng 26*

HIGHLIGHTS

The final project report is complete and addended to this progress report for information and review.

The final total costs of the project are estimated at about $176,000.

PROJECT PROGRESS REPORT FOR DECEMBER 1977
NIOSH STANDARDS EVALUATION OF NICKEL POWDER

INTRODUCTION

The epidemiologic study of K-25 employees who have been occupationally exposed to elemental nickel is essentially complete. As originally planned, the project work was budgeted through December, 1977. Final cost estimates are included in this progress report, the last in the series.

The final report of the project is addended to this progress report. Prepared by the epidemiologist and biostatistician at Oak Ridge Associated Universities (ORAU) contracted to this project, the report shows evidence for no increased risk of mortality due to respiratory cancer among workers exposed to elemental nickel.

The authors of the addended project report and other members of the project staff wish to expedite the acceptance of the final report. Management of UCCND, DOE-ORO, and INCO who have assumed responsibility for review are encouraged to return comments and/or recommended revisions as early as possible. Following final revisions, the project report will be available to the Occupational Safety and Health Administration, which has been advised of the advanced status of this study.

PROJECT COSTS

Although the activities generating costs to this project have been budgeted through December, 1977, some of the charges will not be realized until January because of handling delays. The accounts will remain open for pickup of all costs. An estimate of total project costs has been computed, as presented below:

	Estimated Total Expenditure	Budget	Estimated Percent Expended
Management & Staff	$ 51,700	$ 58,300	89
Oak Ridge Assoc. Univ.	50,000	50,000	100
Computer & Other	17,586	27,700	63
Expense	57,016	64,000	89
	$176,302	$200,000	88

EPIDEMIOLOGIC STUDY - E. A. Tompkins and J. H. Godbold

The final report of the study has been completed, subject to acceptance by the management of UCCND, DOE-ORO, and INCO. As a convenience to those interested in the project and as an expedient in transmittal, the project report has been placed as an addendum to this progress report. Later revisions may be incorporated following review by the above management. Also, minor statistical adjustments may be made later, after the receipt of outstanding death certificates. However, no significant revisions are expected in the findings or conclusions of this study.

This project report will be available to OSHA for their consideration in proposing standards for nickel exposure. Eventually the findings of this epidemiologic study are expected to be represented by a journal publication; but, in view of the crowded nature of journal publishing, this cannot be realized in less than 8 to 12 months.

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K/NI-1, Part 12,
Addendum

A LONG-TERM MORTALITY STUDY OF WORKERS OCCUPATIONALLY EXPOSED TO ELEMENTAL NICKEL AT THE OAK RIDGE GASEOUS DIFFUSION PLANT*

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and

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January, 1978

* Supported by Union Carbide Corporation - Nuclear Division (under contract to the U.S. Department of Energy) and International Nickel Corporation

SUMMARY

This study was undertaken to test the hypothesis of no increased risk of mortality from respiratory cancer among workers occupationally exposed to elemental nickel at the Oak Ridge Gaseous Diffusion Plant (ORGDP) when compared to workers at the same plant with no record of occupational exposure to nickel or its compounds. The data collected over a minimum 20-year period of follow-up show evidence for no increased risk of mortality due to respiratory cancer among the exposed workers. The data also show that the exposed workers experienced somewhat lower mortality than the controls both for deaths due to respiratory cancer and for deaths due to all causes, although neither of these differences is statistically significant. The controls were examined for adequacy, and no gross differences were apparent even though there were suggestions of differences in smoking histories between the exposed workers and the controls.

A LONG-TERM MORTALITY STUDY OF WORKERS OCCUPATIONALLY EXPOSED TO ELEMENTAL NICKEL AT THE OAK RIDGE GASEOUS DIFFUSION PLANT

The first investigations into the health of workers occupationally exposed to nickel or its compounds took place in the early 1930's due to an apparent propensity of workers at nickel smelters and refineries for cancer of the nasal cavities. Since then thorough and carefully controlled epidemiologic studies[1] of respiratory cancer have been conducted among nickel refinery and smelter workers in Wales, Canada, Norway, and Russia. These studies have revealed a significantly increased incidence of cancers of the lung and nasal cavities among the workers, with increased risk of respiratory neoplasia being especially associated with specific operations involving roasting and conversion of nickel sulfide to nickel oxide. Respiratory cancers in nickel workers have usually developed after long latent periods, such as are typical of cancers associated with occupational exposures. However, since the 1930's the technology of nickel smelting and refining has undergone improvements that probably have diminished the risk of respiratory carcinogenesis. There is only scanty evidence reported in the literature of an increased incidence of respiratory cancers among workmen who have other types of occupational exposure to nickel, such as nickel electroplating and grinding.[1]

To date, there have been no reported investigations of workers occupationally exposed to pure elemental nickel, but not to other nickel compounds; and since there exists a population of such workers at the Oak Ridge Gaseous Diffusion Plant (ORGDP)*, a study was undertaken to examine the effect of occupational exposure to elemental nickel on the health of these workers. Exposure to elemental nickel at ORGDP occurs in the manufacture of barrier, a special porous medium employed in the gaseous diffusion enrichment of isotopic uranium.

The study undertaken is a mortality study designed to test the hypothesis that exposure to elemental nickel in this particular working environment has no effect on mortality due to cancers of the respiratory system. To test this hypothesis, the mortality of workers occupationally exposed to elemental nickel in the manufacture of barrier has been compared to that of workers at the same plant who have no record of any occupational exposure to elemental nickel or its compounds during their employment at ORGDP.

In order to make a comparison of the mortality in the two groups, it was necessary to follow each worker in the exposed and control groups from the date of initial hire to either death or the termination of the observational period of the study. The follow-up was facilitated to a large degree by the availability of the data which had been collected for the ERDA Health and Mortality Study. This data-collection system included sending a roster of noncurrent employees for whom there were no death certificates on file to the Social Security Administration.

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* Operated by Union Carbide Corporation - Nuclear Division, under contract to the U.S. Department of Energy.

From their records, Social Security identified those individuals on the roster who were dead; and from this information, searches were made in the various state health departments for the corresponding death certificates. The last submission of a roster to Social Security occurred early in 1974 for those individuals who were noncurrent as of December 31, 1973. Therefore, with this system of identifying deaths in the study population, it was necessary to terminate the observational period for this study on December 31, 1973.

Since the majority of the population of workers in the barrier plant was initially hired before 1954, it was decided to limit study to this group, thereby assuring a minimum twenty-year follow-up period for each exposed individual. From the inception of barrier manufacture at the ORGDP in January, 1948, to December 31, 1973, there have been 929 employees whose work history shows a department code identifying them as barrier workers. Of these 929 employees, 852 were initially hired into or transferred into the barrier plant before January 1, 1954; and of these 852 employees, there were 814 white males and 38 white females. Furthermore, since all the deaths due to respiratory cancers occurred among white males, statistical analysis was restricted to these 814 individuals.

The control group for the study was obtained by drawing a 25 percent sample of all white male employees at ORGDP with no record of occupational exposure to nickel or its compounds in this plant (or in other UCC-ND plants) and whose period of active employment included at least one day in the period January 1, 1948, through December 31, 1953. By being selected in this way, these employees had the potential for being hired into or transferred into the barrier plant during the same time period as the exposed population. The 25 percent sample yielded a total of exactly 1,600 white male employees.

CAUSES OF DEATH

Once the study population was identified, each individual was followed until either death or termination of the observation period, December 31, 1973, by the method earlier described. This follow-up resulted in the identification of 90 deaths among the 814 exposed workers and 284 deaths among the 1,600 controls. For the 90 deaths among the barrier plant workers, death certificates were located for all except one individual. For this person, Social Security provided information that the death was a military casualty of the Vietnam War. A death certificate was unable to be obtained from the Department of Defense without a military service number, but the death has been classified as a military casualty. For the 284 deaths among the controls, death certificates have been obtained for all except 11 individuals.

These deaths for both exposed (nickel worker) and control groups are displayed by cause in Table 1 under the heading *observed* deaths. The 11 deaths for which death certificates have not yet been obtained have been distributed (as a temporary statistical propriety) among the causes of death in the same proportions as those 273 deaths for which certificates were obtained, yielding fractional numbers of observed deaths among the controls. This allocation was done under the assumption that the distribution of the causes of the 11 deaths with no certificates does not differ from that of the 273 deaths with certificates.

Since the cause of death under investigation, cancer of the respiratory system, is one for which the probability of death is extremely low, few deaths would be expected to be due to this cause in either the exposed or the control groups.

Table 1

OBSERVED AND EXPECTED DEATHS BY CAUSE FOR NICKEL WORKERS AND CONTROLS

	NICKEL WORKERS		CONTROLS	
	Observed	Expected	Observed	Expected
ALL CAUSES	90	122.78	284.00	354.25
Infective and Parasitic Diseases	0	1.80	2.08	5.70
Malignant Neoplasm	18	22.39	54.09	65.75
Buccal Cavity and Pharynx	2	.80	1.04	2.31
Digestive Organs and Peritoneum	3	6.01	11.44	19.18
Respiratory System	3	7.52	24.97	21.44
Nasal Sinus	0	*	0.00	*
Bone, Connective Tissue, Skin, and Breast	2	1.03	1.04	2.49
Malignant Melanoma	2	.53	0.00	1.25
Genitourinary Organs	3	2.08	5.20	7.28
Other and Unspecified Sites	2	2.26	5.20	6.12
Lymphatic and Hematopoietic	3	2.69	5.20	6.93
Benign Neoplasm and Neoplasm - Nature Unspecified	1	.43	0.00	1.09
Endocrine, Nutritional, and Metabolic Diseases	4	2.06	1.04	5.91
Diseases of Blood and Blood-Forming Organs	0	.25	2.08	.78
Mental Disorders	0	.89	4.16	1.97
Diseases of Nervous System and Sense Organs	0	1.22	2.08	3.07
Diseases of Circulatory System	38	57.84	151.88	181.75
Diseases of Respiratory System	5	5.88	14.56	18.65
Diseases of Digestive System	4	7.49	3.12	19.36
Diseases of Genitourinary System	1	1.67	6.24	5.16
Diseases of Skin and Subcutaneous Tissue	0	.09	0.00	.25
Diseases of Musculo-Skeletal System and Connective Tissue	0	.23	0.00	.61
Congenital Anomalies	0	.42	0.00	.88
Symptoms and Ill-Defined Conditions	6	1.50	7.28	3.88
Accidents, Poisonings, and Violence	13	18.62	35.36	39.44
All Accidents	6	13.02	22.88	27.56
Motor Vehicle Traffic Accidents	3	6.40	13.52	12.90
Water Transport Accidents	0	.39	1.04	.76
Air and Space Transport Accidents	0	.55	2.08	.97
Accidental Drowning	1	.53	1.04	1.11
Other Accidents	2	5.15	5.20	11.82
Medical Misadventure	0	.15	1.04	.38
Suicide	6	4.25	7.28	9.31
Homicide	0	1.18	4.16	2.24
Military Casualty	1	*	0.00	*

* Unable to be calculated from Vital Statistics data.

Associated with a small number of observed deaths from such a cause is a relatively large amount of variability. Ratner than compare the observed deaths due to cancer of the respiratory system in the exposed group directly to the corresponding observed deaths in the control group, it was decided to compare the two groups indirectly by comparing each of them directly to the observed deaths in the U.S. white male population.[2] Since the national population is as large as it is, it contains virtually none of the variability present in smaller populations.

The direct comparison of each group of workers to the U.S. white male population was done by calculating an expected number of deaths for that group based on national mortality rates and then forming the ratio of the observed number of deaths to the expected number of deaths to give a Standard Mortality Ratio (SMR) for cancers of the respiratory system.* It is easily seen that should the observed number of deaths due to respiratory cancer for either group turn out to be equal to the expected number, then the SMR for respiratory cancers for that particular group would be 1.00. For each group, the expected number of deaths is calculated by applying the age-, sex-, race-, year-, and cause-specific mortality rates in the U.S. population to the age- and year-specific person-years at risk in that particular group of the study population, thereby adjusting for any differences in age or time of survival between the two groups. The calculation of expected numbers of deaths and the resulting SMR's was necessary only for Malignant Neoplasms: Respiratory System since that was the only cause of death under test. From Table 1, the SMR's for respiratory cancer for the nickel barrier workers (3/7.52) and the controls (24.97/21.44) are calculated to be 0.40 and 1.16, respectively. (For nasal sinus cancer, a special form of respiratory cancer, there were no observed deaths for either group.) Since in Table 1 the observed deaths have been tabulated by cause, expected numbers of deaths have also been calculated for all remaining causes of death and are displayed there along with the observed numbers of deaths for the sake of completeness.

ADEQUACY OF CONTROLS

Since the SMR's for the exposed nickel workers and controls are calculated separately, each on the basis of the U.S. population, primary interest then focuses on the difference between the two SMR's for deaths due to respiratory cancer; i.e., 0.40 for nickel workers and 1.16 for controls. This difference can be evaluated statistically by forming a confidence interval for each SMR. By use of the method described by Haenszel et al.[3] for calculating 95 percent confidence intervals, the interval for exposed workers is (0.08, 1.17), while that for the controls is (0.75, 1.72). On the basis of this analysis, it is seen that there is no statistically significant difference between the two groups.

However, even though the two groups do not differ statistically, the fact that the SMR for respiratory cancers for the nickel barrier workers is 0.40, while that for the controls is 1.16, raises the question of the adequacy of this particular group of controls. In other words, are these two groups of employees similar in all respects relating to the outcome under investigation, or are there differences between them that could account for this observed difference in SMR's?

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* Strictly speaking, SMR's can be compared only for those causes of death for which the study was designed. Other SMR's cannot be compared validly because of their interdependence.

The question could alternatively be asked, with a different emphasis, as: Are there differences between the two groups that could cause a masking of a statistically significant result? Three indicators will be used in an attempt to answer this question: overall mortality, smoking histories, and socioeconomic status.

OVERALL MORTALITY

The reason for using overall mortality for assessing the adequacy of the controls is that it provides a measure in a general sense of the propensity for dying by individuals in the two groups. For example, white females would be a poor control group for this population of white males because overall they experience a lower age-specific mortality rate. The fact that the cause of death under test in this study, i.e., respiratory cancers, is included in the *All Causes* category is not of real concern because this cause is a relatively rare one; and even if there were a detectable difference in this cause due to occupational exposure to elemental nickel, the overall mortality for the two groups should be similar, all other things being equal. From Table 1 the SMR's for deaths from *All Causes* are calculated to be 0.73 for the nickel workers and 0.80 for the controls. The 95 percent confidence intervals are (0.59, 0.91) for the nickel workers and (0.71, 0.97) for the controls; and, as before, there is no statistically significant difference between these two groups. The fact that the SMR's are so similar lends support to the claim that the control group is an adequate control with respect to the underlying force of mortality; the fact that they differ in the same direction for *All Causes* as they do for *Malignant Neoplasms: Respiratory System* suggests the possibility that a selection bias may have been involved in the hiring or transferring of healthier people into the barrier plant or that something associated with employment in the barrier plant acts in a protective way on the health of these workers. Also, the SMR's (with their confidence intervals) for deaths from *All Causes* point out that both groups of workers appear to be somewhat healthier than the general U.S. white male population. There are at least three possible explanations for such a finding. The first is the active preventive medicine program which has been in effect at ORGDP since the opening of the plant. The second is the possibility of under-reporting of deaths by Social Security; and the third is the so-called *healthy-worker effect*,[4] compared to the general population.

SMOKING HISTORIES

The second area of assessing the adequacy of this particular group of controls is the comparison of their smoking histories to the smoking histories of the nickel barrier workers. The reason for this comparison is the long-recognized association between cigarette smoking and respiratory cancers; and, thus, differences in smoking habits between the two groups could help to account for differences or lack of differences in deaths due to respiratory cancer. At the time of initial hire of each individual in this study (i.e., on or before December 31, 1953), no question was asked the employee for the medical record concerning smoking habits. However, in 1955 the use of the Cornell Medical Index Health Questionnaire, which contained the question, *Do you smoke more than 20 cigarettes a day?* was instituted. For each employee in the study, the first response to this question appearing in his medical record was used; for some employees, this question was not answered because of termination prior to 1955.

The percentage distribution of responses for the two groups is shown in Figure 1.* From these data, it is seen that the two groups are comparable in the percentage answering the question *Yes*, but that more nickel workers than controls answered the question *No*. This difference is compensated for by a higher percentage of controls having no answer to the question. If those persons for whom smoking histories are not available are similar in their smoking habits to those for whom smoking histories are available (there is no evidence to indicate otherwise), then there would be a larger proportion of smokers in the control population than in the barrier workers. If such were the case, this could account for the higher SMR for respiratory cancers in the control group. However, if those persons for whom questionnaires are not available differ in their smoking habits from those for whom questionnaires are available, then it is possible for the larger proportion of smokers to be in either group. As a result of such a large number of workers in the *unknown* category, it is not possible to draw definitive conclusions about the influence of smoking habits on the reported mortality of workers in this study.

SOCIOECONOMIC STATUS

The third area of comparison of the controls to the nickel barrier workers is that of socioeconomic status. This comparison is a natural one since lower socioeconomic groups have been shown to experience higher mortality rates for respiratory cancer than the higher groups.[5] The two indicators of socioeconomic status which will be used on this population are *length of employment* and *payroll status*. In Figure 2 the percentage distributions for length of employment** of the two groups of workers are displayed by five-year intervals. These data show that there are more controls in each of the extreme categories; i.e., the 0-4 year period† and the 25-29 year period (as well as the final year)††. A shorter length of employment would indicate lower socioeconomic status; while a longer period would indicate higher status. Thus, these data indicate that the control group is a more heterogeneous group than the barrier workers with respect to this particular indicator.

Regarding payroll status, on each employee's personnel record a notation of his payroll status at time of initial hire is entered as hourly, weekly, or monthly. Each time subsequent to this that his payroll status changes, notation is again entered on the personnel record. From these data, it is possible to derive seven combinations of the payroll status categories, disregarding ordering within each combination. The seven combinations are the following: hourly, weekly, monthly, hourly-weekly, hourly-monthly, weekly-monthly, and hourly-weekly-monthly. The percentage distributions for the two groups of workers by the seven combinations of payroll status are shown in Figure 3. These data show the nickel

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* In a number of medical records, in lieu of the Cornell Questionnaire, a company form provided equivalent information on smoking habits.

** Some employees of both groups were employed at other sites for the same employer during the period of observation, 1948-1973.

† The 0-4 year period goes up to, but does not include, the 5th anniversary.

†† This is the year after the 30th anniversary. The full employment period studied is from 1943 through 1973, a total of 31 years.

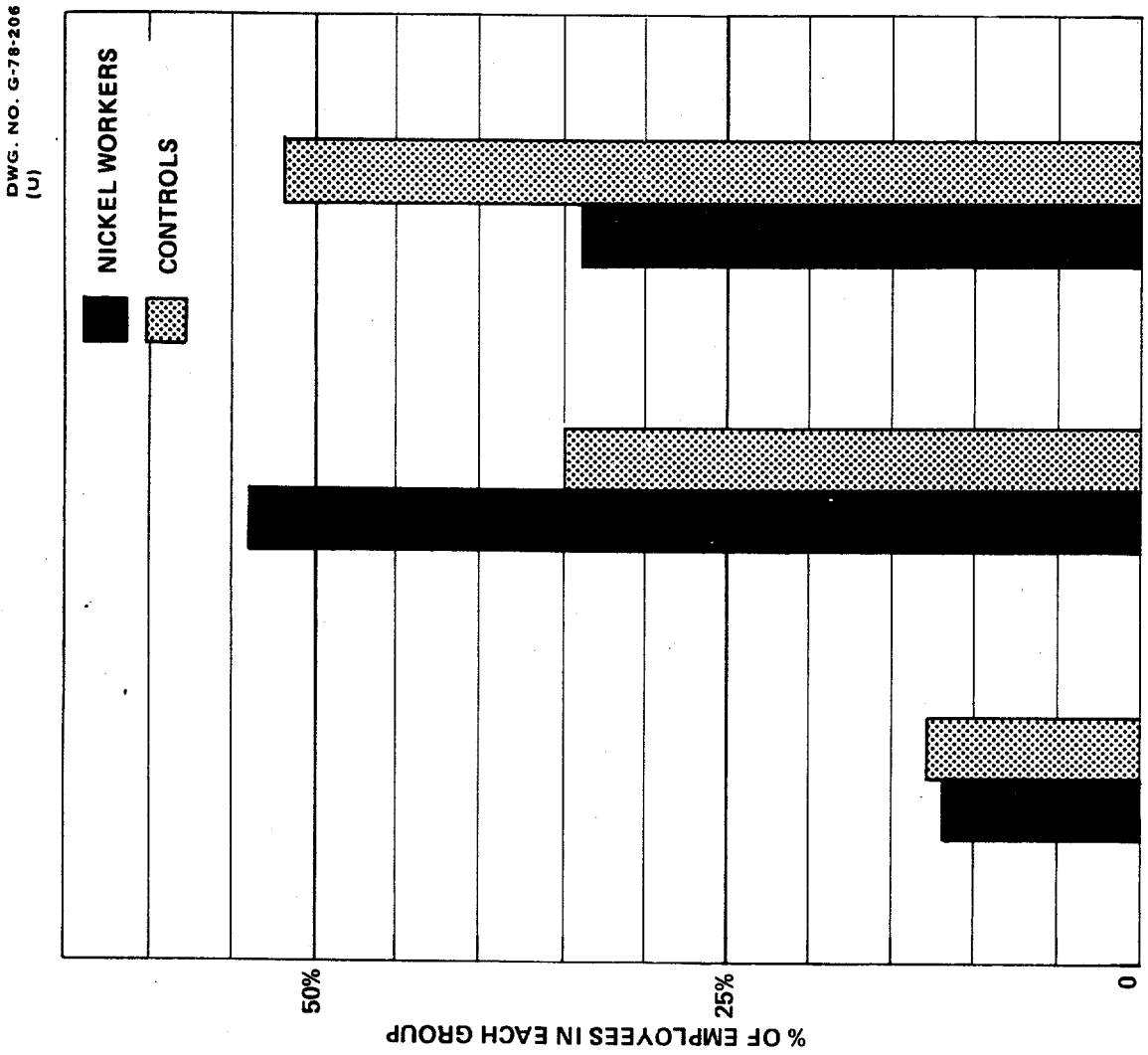

Figure 1
SMOKING HISTORIES OF NICKEL WORKERS AND CONTROLS

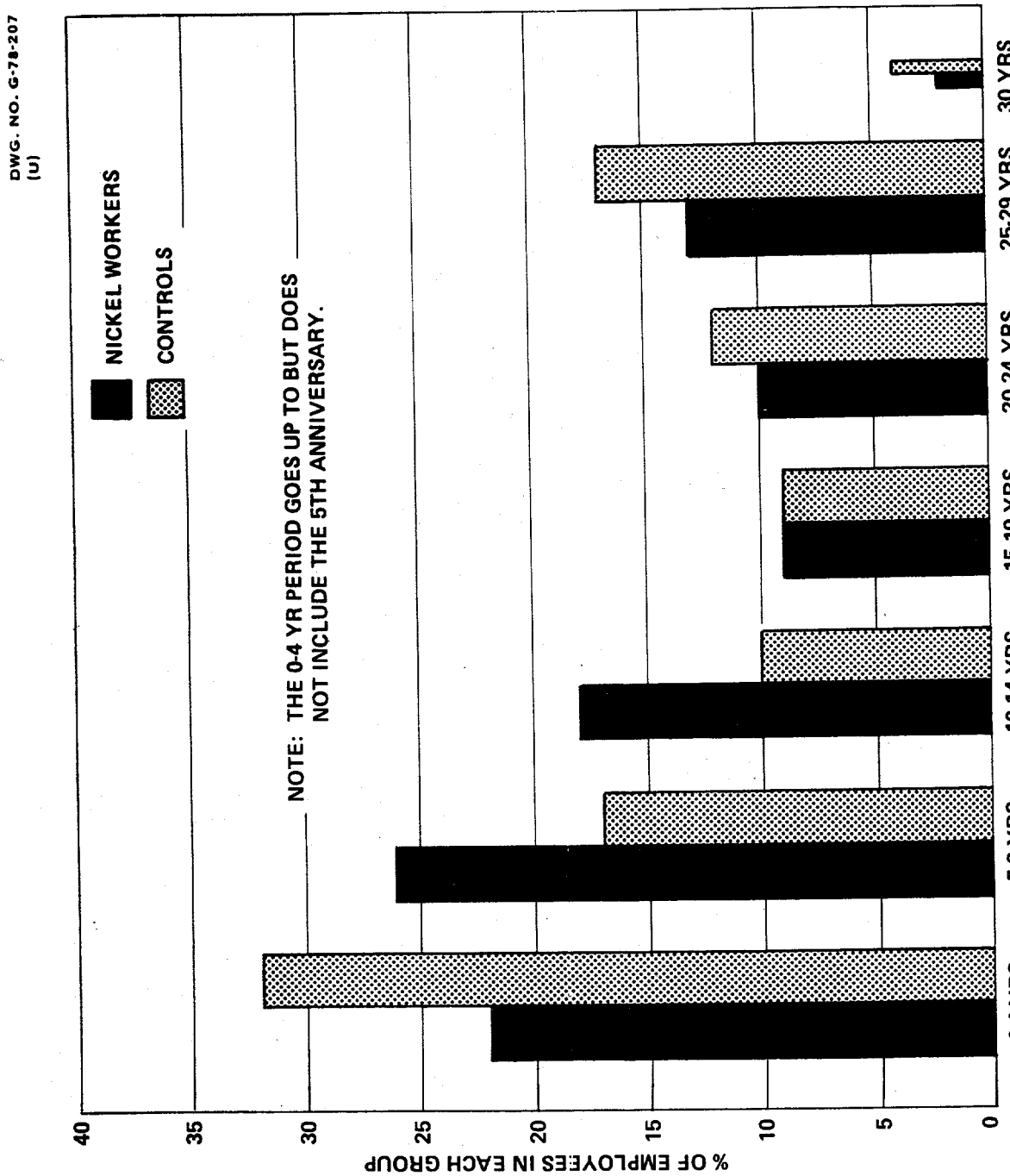

Figure 2

LENGTH OF EMPLOYMENT FOR NICKEL WORKERS AND CONTROLS

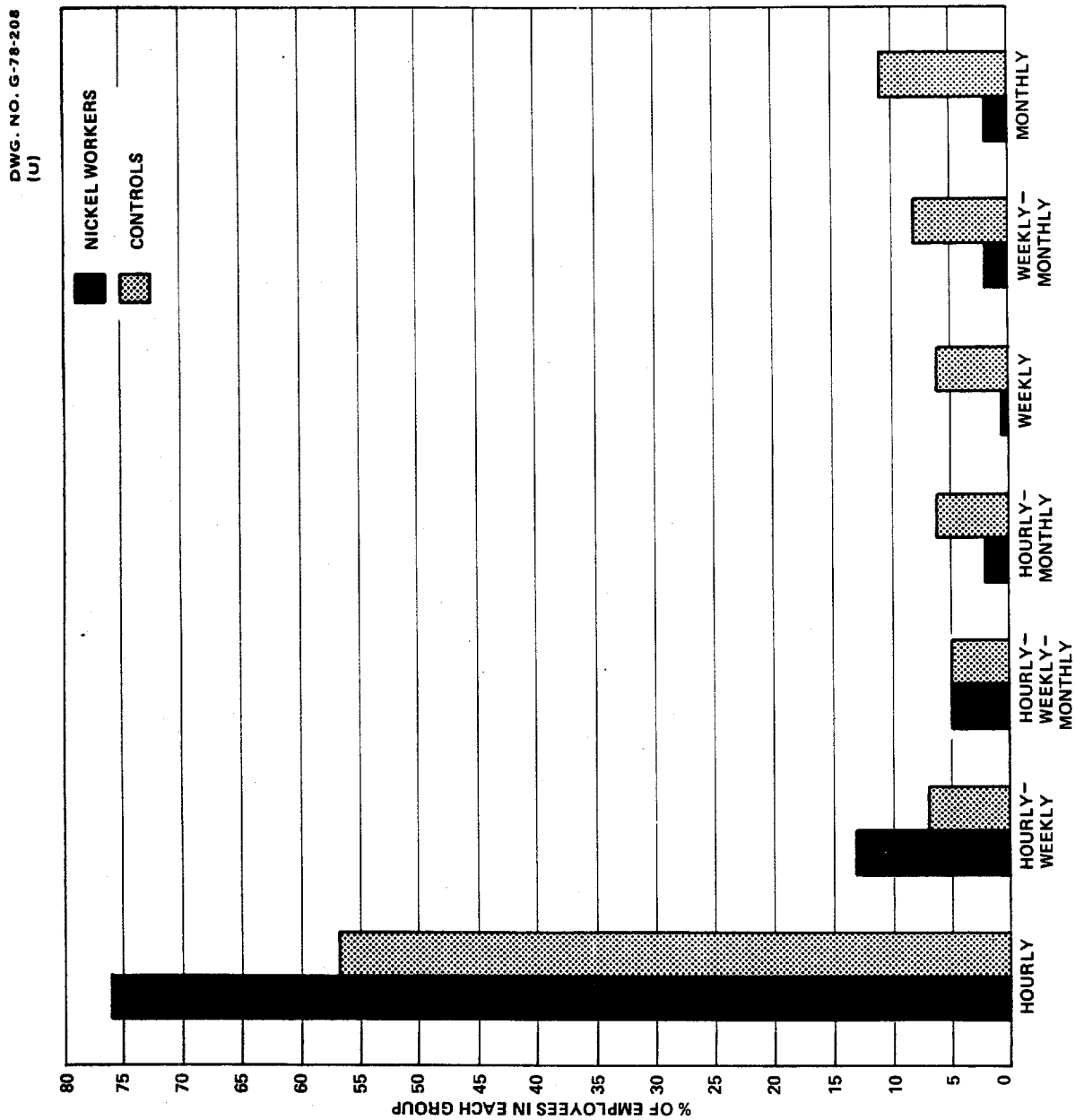

Figure 3

PAYROLL STATUS FOR NICKEL WORKERS AND CONTROLS

workers exceeding the controls percentage-wise in the hourly and the hourly-weekly combinations, near equality for the hourly-weekly-monthly combination, and the controls exceeding the nickel workers in the four remaining combinations. This analysis supports the view that the controls are a more heterogeneous group socioeconomically; the nickel workers are about 90% hourly and hourly-weekly employees, whereas the controls are about 64% in those two categories. The nickel workers would seem, therefore, to be a lower socioeconomic group, if anything, than the controls. This finding is directionally inconsistent with the lower respiratory cancer mortality among the nickel workers; and, thus, does not appear to be its explanation.

Now that the controls have been compared to the nickel barrier workers for adequacy with respect to overall mortality, smoking history, and socioeconomic status, the data do not show them to be grossly inadequate in any particular respect. The general mortality data support the directional trend of the nickel workers' being the healthier group; the smoking data could possibly account for the differential respiratory cancer mortality if, in fact, the controls as a group are heavier smokers; the socioeconomic data indicate more heterogeneity among the controls with indications of the nickel workers' being a lower socioeconomic group, a finding directionally inconsistent with the mortality data previously examined.

MAXIMUM RISK

Even though the data do not show a statistically significant difference between the exposed group of workers and either the in-plant controls or the U.S. white male population with regard to respiratory cancer mortality, the question arises as to what is the maximum risk with which the observed data for the exposed workers is consistent. Using tables of the Poisson distribution,[6] it is seen that an expected number of deaths from respiratory cancer of greater than 7.76 in the nickel barrier workers would make the observed number of three cases significantly low. Since the expected number of deaths for this cause based on U.S. white male experience is 7.52, we see that the data show good evidence for no increased risk in respiratory cancer among the nickel barrier workers over that expected on the basis of national experience. Since the in-plant controls experienced more respiratory cancer deaths than expected based on U.S. white male data, it can also be said that data collected in this study provide good evidence for no increased risk of mortality due to respiratory cancer on the part of the nickel barrier workers over that expected on the basis of the in-plant controls.

OTHER OBSERVATIONS

In addition to the particular cause of death under investigation, several other observations on the data in Table 1 are worth mentioning. Although both groups are running below expectancy in Diseases of the Circulatory System, the controls are experiencing higher mortality than the nickel barrier workers. Higher mortality of controls also applies to Mental Disorders. Areas where the nickel barrier workers are experiencing higher mortality than the controls are cancers of the Buccal Cavity and Pharynx, Malignant Melanoma, and Symptoms and Ill-Defined

Conditions. It is not within the scope of this investigation to probe further into these particular causes, but further study might prove to be of interest.

For the sake of completeness: there was only one observed death occurring among the 38 white female nickel workers employed during the period of study; it was due to Malignant Neoplasm: Digestive Organs and Peritoneum.

NICKEL EXPOSURES

Another area of inquiry in this study was the levels of nickel to which the barrier workers were exposed. The ORGDP Industrial Hygiene Department reviewed all available plant records that could potentially provide data descriptive of occupational exposures to nickel in the barrier manufacturing facilities. Emphasis was placed on obtaining data collected during the period 1948-1973. The data presented in Table 2 represent more than 3,000 air-monitoring samples collected in the Barrier Manufacturing Plant from 1948 through 1963. No air-monitoring data were located for the years 1964-74, due to the fact that in 1963 and until 1975, the industrial hygiene monitoring functions were the responsibility of the various plant operating divisions; and sampling was performed only on an *as-needed* basis. Biological monitoring records (urinalysis) were reviewed but judged to be inadequate for use as indicators of occupational exposure to nickel.

CONCLUSION

In conclusion, this study was undertaken to test the hypothesis of no increased risk of mortality from respiratory cancer among workers occupationally exposed to elemental nickel at ORGDP when compared to workers at the same plant with no record of occupational exposure to nickel or its compounds. The data collected over a minimum twenty-year period of follow-up show evidence for no increased risk of mortality due to respiratory cancer among the exposed workers. The data also show that the barrier plant workers experienced somewhat lower mortality than the controls both for deaths due to respiratory cancer and for deaths due to all causes, although neither of these differences is statistically significant. The controls were examined for adequacy, and no gross differences were apparent even though there were suggestions of differences in smoking histories between the exposed nickel workers and the controls.

Table 2. LEVELS OF NICKEL FROM AIR SAMPLES IN THE BARRIER MANUFACTURING PLANT (1948-1963)

Location	N[1]	Mean[2]	Range[2]	Standard Deviation[2]	Sample Duration Mode in Min.
Manufacturing Areas:					
M-1	2,220	2.19	0-566.0	18.55	30
M-2	219	13.30	0-459.0	48.49	60
M-3	217	1.33	0-140.8	9.81	60
M-4	17	0.19	0- 1.00	0.25	30
Support Areas:					
S-1	328	1.06	0-103.1	6.62	30
S-2	4	0.28	0- 1.00	0.49	30
S-3	4	0.08	0- 0.10	0.05	30
S-4	3	0.00	0-0	0	30
S-5	29	0.43	0- 6.90	1.31	30
S-6	13	4.99	0- 62.90	17.40	150
S-7	4	0.05	0- 0.20	0.10	30
S-8	8	0.00	0-0	0	30
S-9	6	0.00	0-0	0	390

[1] Number of Samples Collected.

[2] Data expressed in mg/m^3 of air.

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Title and author (if document is unnumbered) (5 documents)

Rec (1) ~~*~~ Updated Study of DOE-UCC/ND Nickel Workers at K-25 and attachment (C C Lushbaugh) DRAU, 1/31/80

Co (2) Attachment to Item 1 — Letter to S S Stiff from A Warner, Inco Limited, dated 3/7/80

(This section to be completed by Document Center)

Date request received 1/22/96

Date submitted to ADC 1/25/96

Date submitted to HSA Coordinator 1/22/96

(This section to be completed by HSA Coordinator)

Date submitted to CICO 1/25/96

Date received from CICO 1/30/96

Date submitted to ChemRisk/Shonka and DOE 1/30/96

(This section to be completed by ChemRisk/Shonka Research Associates, Inc.)

Date document received _____

Signature _____

Rec (3) Letter to LA Dean, et al., from J A Barker, dated 12/21/79, A Long-Term Mortality Study of ORGDP Barrier Workers Exposed to Metallic Nickel (W/O Attachment)

Co (4) Letter to Ad Hoc Inorganic Nickel Committee & Dr. K. Lane dated 5/15/79, from H L Hayes, Chemical Selection Subgroup of the Clearinghouse on Environ. Carcinogens Mtg May 25, 1979 (W/O Attach)

Co (5) Attachment to Item 4, Dept of HEW, Minutes, fifteenth Mtg of Chemical...

From Box
12-2-3-16

UPDATED STUDY OF DOE/UCC-ND NICKEL WORKERS AT K-25

The initial study of the mortality experience of barrier workers exposed to metallic nickel aerosols was recently reported at length in the Journal of Occupational Medicine (A Long-Term Mortality Study of Workers Occupationally Exposed to Metallic Nickel at the Oak Ridge Gaseous Diffusion Plant, J. Occup. Med. 21, 799-806, 1979 by Dr. J. H. Godbold, Jr. and E. A. Tompkins). This study based on an SSA ascertainment of death up to 1973 will be extended to include other decedents up to December 1978 when this SSA search is completed. Dr. Anthony Polednak, consultant epidemiologist to ORAU, has agreed to provide scientific overview of this effort. Past experience suggests that a realistic time-frame for planning purposes is (a) completion of SSA search, March 1980; (b) completion of death certificate searches by state, July 1980; (c) completion of internal review of initial study to determine the applicability of recently automated biostatistical analysis programs, March 1980; (d) completion of construction of analysis files, August 1980; (e) epidemiologic and biostatistical analysis of updated data, early September 1980; (f) completion, internal review (UCC-ND/ORAU) of preliminary report, late September 1980; final report, October 1, 1980. Point of contact within ORAU for progress reports on an as-needed basis are: C. C. Lushbaugh, program director; B. Dupree, on-site epidemiologist; E. Frome, biostatistical analyst.

C. C. Lushbaugh
1-31-80

Prepared by the Oak Ridge Associated Universities for Union Carbide Corporation-Nuclear Division, operating contractor for the U.S. Department of Energy under U.S. Government Contract No. W-7405-eng-26.

ChemRisk/Shonka Research Associates, Inc., Document Request Form

From Box 12-2-3-16

(This section to be completed by subcontractor requesting document)

J. Lamb / 1034A
Requestor / Document Center (is requested to provide the following document)

Date of request ~~12/8/95~~ 1/96 Expected receipt of document 1/8/95

Document number _____ Date of document 1/31/80

Title and author (if document is unnumbered) (5 documents)

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Date received from CICO 1/30/96

Date submitted to ChemRisk/Shonka and DOE 1/30/96

(This section to be completed by ChemRisk/Shonka Research Associates, Inc.)

Date document received _____

Signature _____

Rel (3) Letter to L A Dean, et al., from J A Barker, dated 12/21/79, A Long-Term Mortality Study of 10,000 Barrier Workers Exposed to Metallic Nickel (w/o Attachment)

CO (4) Letter to Ad Hoc Inorganic Nickel Committee & Dr. K. Lane dated 5/15/79, from H L Haynes, Chemical Selection Subgroup of the Clearinghouse on Environ. Carcinogens Mtg May 25, 1979 (w/p Attach)

CO (5) Attachment to Item 4, Dept of HEW, Minutes, Fifteenth Mtg of Chemical...

UNION CARBIDE

NUCLEAR DIVISION

INTERNAL CORRESPONDENCE

December 21, 1979

L. A. Dean, K-1035, MS 219
P. C. Fourney, 9704-2, MS 005, Y-12
R. G. Jordan, 9704-2, MS 021, Y-12
A. J. Legeay, K-303-7, MS 337
R. W. Levin, K-1004-A, MS 434
J. R. Merriman, K-1004-A, MS 428
K. W. Sommerfeld, K-1001, MS 134
S. S. Stief, K-1001, MS 141
F. Strang, K-1037, MS 349

A Long-Term Mortality Study of ORGDP Barrier Workers Exposed to Metallic Nickel

I thought you would be interested in the attached article which appeared in the December, 1979, issue of Journal of Occupational Medicine. As indicated, the study revealed very positive results.

J. A. Barker

J. A. Barker, K-1001, MS 137 (4-8317)

JAB:ph

Attachment

cc: T. G. Fortney, K-1003, MS 422

cc/att: File - JAB (NoRC)

Prepared by Union Carbide Corporation-Nuclear Division, operating contractor for the U.S. Department of Energy under U.S. Government Contract No. W-7405-eng-26.

ChemRisk/Shonka Research Associates, Inc., Document Request Form

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Date submitted to HSA Coordinator 1/22/96

(This section to be completed by HSA Coordinator)

Date submitted to CICO 1/25/96

Date received from CICO 3/4/96

Date submitted to ChemRisk/Shonka and DOE 3/4/96

(This section to be completed by ChemRisk/Shonka Research Associates, Inc.)

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Signature _____

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CO (5) Attachment to Item 4, Dept of E/EW, Minutes, Fifteenth Mtg of Chemical...

UC 249-2

cc: R. D. Gilmore (2) 9/6/79
R. A. Winkel/K. W. Sommerfeld
S. S. Stief 8-22-79
(3) J. A. Barker 9/24

gkb 9/7/79

UNION CARBIDE

INTERNAL CORRESPONDENCE

K.W. SOMMERFELD

RELATIONS DIVISION

J. A. BARKER

SEP 6 9 05 AM '79 SEP 7 9 03 AM '79

UNION CARBIDE CORPORATION 270 PARK AVENUE, NEW YORK, NEW YORK 100

To (Name) Division Location Floor Number	Ad Hoc Inorganic Nickel Committee & Dr. K.S. Lane	Date	August 15, 1979
		Originating Dept.	HS&EA
		Floor Number	22
Copy to	GOHC	Answering letter date	
		Subject	Chemical Selection Subgroup of the Clearinghou on Environmental Carcinoge Meeting May 25, 1979

For your information refer to Page 3 and the relative listings of the nickel compounds in Attachment I. Nickel Sulfate and Nickel Oxide are given high ranking as compared with a low ranking for Nickel Dust.

H. L. Haynes

H.L. Haynes

Attachments
HLH:cjm

ChemRisk/Shonka Research Associates, Inc., Document Request Form

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DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service
National Institutes of Health
National Cancer Institute
Division of Cancer Cause and Prevention
Bethesda, Maryland

Nicholas Hoe

MINUTES*

Fifteenth Meeting of the Chemical Selection Subgroup of the
Clearinghouse on Environmental Carcinogens
May 25, 1979
Building 31 Conference Room 7

* These minutes have not been approved by the Chemical Selection Subgroup of the Clearinghouse on Environmental Carcinogens.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service
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MINUTES

Fifteenth Meeting of the Chemical Selection Subgroup of the
Clearinghouse on Environmental Carcinogens
May 25, 1979
Building 31 Conference Room 7

Chemical Selection Subgroup Members Present

David B. Clayson (Chairman), Eppley Institute for Cancer Research
Norton Nelson, New York University Medical Center
Verne A. Ray, Pfizer Medical Research Laboratory
Kenneth Wilcox, Michigan State Health Department
James M. Sontag (Executive Secretary), NCI

Chemical Selection Subgroup Members Absent

William Lijinsky, Frederick Cancer Research Center
Paul O.P. Ts'o, Johns Hopkins University

Ad Hoc Members Present

Winston deMonsabert, FDA

Program Reviewers

T. Cameron, NCI
David Gould, EPA
A. Gregory, NIOSH
H. Kraybill, NCI
J. Sevin, NIOSH
Elizabeth Weisburger, NCI

Other NCI Staff Present

I.C. Blackwood
J.F. Douglas
Richard Griesemer
C.K. Grieshaber
W.V. Hartwell
C.W. Jameson
Carolyn Lingeman
Caroline Webb

Guests Present

Chris Connor, EPA
Victor Fung, SRI International
Neil Froemming, Chemical Regulation Reporter
Harry Hays, USDA
Laura Owen, Toxic Material News
Peter A. Pearl, Gillette Co.
Judy Patt, Biospherics
Patrick Siu, FDA
M.J. Sloan, Shell Oil Co.
J. Stauee, Biospherics
2 Unidentified Guests

I. Call to Order

Dr. Clayson opened the fifteenth meeting of the Chemical Selection Subgroup of the Clearinghouse on Environmental Carcinogens. The minutes of the fourteenth Subgroup meeting were approved as written.

Dr. Nelson remarked on a letter received from Dr. Lloyd Tepper of Air Products and Chemicals. Dr. Tepper took exception to the statement in the minutes of the last meeting attributed to Dr. Nelson concerning ".... polyvinyl chloride latex .... a component of water-based paints ...." In the letter, Dr. Tepper states ".... that there is no commercially available paint based on polyvinyl chloride emulsions." Dr. Nelson indicated that he did not know the correctness of this assertion.

There was no response to a call for public statements.

II. Report on Clofibrate

Dr. Clayson noted that Clofibrate had been selected earlier with low priority by the NCI Chemical Selection Working Group (CSWG). It was subsequently deferred by the Clearinghouse Subgroup in order to determine the FDA's interest in the substance and to clarify the previous test data. The FDA informed the CSWG that it was reviewing the animal studies and recommended no further testing at present.

III. Chemical Nominations

METAL CLASS

Nickel Sulfate, Nickel Oxide, and Nickel Dust. Based on the information received from Dr. E. Mastromatteo of INCO Limited, Dr. Clayson suggested Nickel Sulfate, Nickel Oxide and Nickel Dust all be considered by the Subgroup. Dr. Gregory commented on the difficulty of identifying the specific nickel compound(s) posing a human cancer risk. He noted that exposure to nickel fumes was an important occupational problem.

Dr. Clayson said that major determinants in selecting the appropriate nickel derivative were bioavailability and route of exposure. Because of the ill-defined nature and workplace variability of Nickel Dust, he opined that it should be given a lower test priority than Nickel Sulfate and Nickel Oxide. Dr. Nelson noted that the compounds may become bioavailable in different ways, based on their solubility. He agreed that Nickel Sulfate and Nickel Oxide should receive the highest priority and that the emphasis should be on inhalation exposure. Dr. Nelson suggested that lung implant studies might be an inexpensive, comparative means of studying the range of suspected nickel compounds. Dr. Clayson recommended that nickel fumes and nickel dust be considered again when more specific data on them were available for discussion.

Dr. Sev[illegible]oted an epidemiologic study in which workers and the local populatio[illegible] associated with an Indonesian nickel ore smelter were at an excess lung cancer risk. Although the Nickel Sulfide was produced, she said the oxide was exhausted into the air.

On a linear (1 to 10) scale of progressive priority, Nickel Sulfate received a mean testing score of 8.0; Nickel Oxide a mean testing score of 7.2; and Nickel Dust a mean testing score of 3.2.

Selenium. Dr. Kraybill said a question existed about earlier studies suggesting that Selenium may be carcinogenic. Other studies have shown Selenium to have a tumor inhibitory activity. Selenium exposure may occur by different routes, including ingestion and inhalation. It was noted that Selenium is an essential element at physiologic levels. The CSWG selected Selenium with high priority.

Dr. Clayson noted a recent NCI study showing Selenium Sulfide to be carcinogenic in rats and mice (DHEW Publication No NIH-79-1750). He recommended that more information was needed about the metabolism of Selenium itself before deciding if a carcinogenicity study should be undertaken. Metabolism studies are essential to determine absorption and distribution of Selenium at high levels, since peak exposures constitute the major concern. Dr. Clayson opined that levels of Selenium

in drinking water were sufficiently low as not to present particular concern. He recommended that Selenium be given low priority unless evidence showed significant absorption at high exposure levels. Dr. Nelson agreed that metabolic studies should be done, though he was uncertain as to the most meaningful type of carcinogenicity study. He suggested that Selenium should recieve low priority if tested by routine procedures. Dr. Clayson recommended that a research effort was needed to investigate Selenium, rather than a simple test of its carcinogenicity.

Dr. Wilcox noted that the major occupational hazard probably is not from Selenium itself but rather from some forms of Selenium, which likely vary in solubility. Dr. Gregory confirmed that occupational exposure may be to several different forms of Selenium. Exposure to Selenium itself comes from grinding operations or fumes from vaporization, although exposure by these ways affect a relatively limited number of workers.

On a linear (1 to 10) scale of progressive priority, Selenium received a mean testing score of 2.2.

Ferroselenium. Dr. Kraybill indicated that Ferroselenium was nominated by the CSWG based on the lack of chronic toxicity data and on the compound's high production volume. He noted the possibility of iron and selenium blood levels increasing when Ferroselenium was used as a component of steel implants.

Dr. Clayson questioned the need to test Ferroselenium, given the fact that Selenium Sulfide already has been shown to be carcinogenic. A discussion ensued regarding the feasibility of lowering the regulatory standard for Ferroselenium if the compound was found to be carcinogenic. Dr. Clayson said there was an inadequate amount of biological data on Ferroselenium on which to determine the need to test the compound. It was pointed out that the TLV on Ferroselenium was established more on empirical than hard data. On a linear (1 to 10) scale of progressive priority, Ferrorselenium received a mean testing score of 3.1.

Sodium Selenite. Dr. Gregory said Sodium Selenite was nominated based on the general carcinogenic suspicion of selenium compounds; a preliminary but inadequately controlled study, showing hepatomas in rats orally administered the compound; and an increasing production trend. He added that occupational exposure to Sodium Selenite has not been shown to be a hazard. Sodium Selenite has been demonstrated to inhibit tumor production by various carcinogens and also to be mutagenic.

Dr. Nelson said that Sodium Selenite should be considered as part of the general selenium issue, particularly with respect to dietary intake. He did not view occupational exposure to Sodium Selenite to be a serious problem and, in this regard, gave the compound a low testing priority.

Despite interesting scientific questions for testing the compound, on more practical grounds, Dr. Clayson agreed that Sodium Selenite should be given a low testing priority. He also thought it should be considered as part of the general selenium issue. It was pointed out that selenized yeast is used as a growth promoter in animal feed. On a linear (1 to 10) scale of progressive priority, Sodium Selenite received a mean testing score of 4.1.

Sodium Dichromate. (This compound was originally presented as Sodium Chromate.) Dr. Gould said that Sodium Chromate was given moderate priority by the CSWG based on its human exposure, suspicion of carcinogenicity, and the fact that it represented a soluble chromium (VI) compound. He noted that the testing of Sodium Chromate would be an attempt to identify the chromium compound associated with increased cancer rates in workers exposed to mixtures of chromium compounds. Dr. Gould indicated that Sodium Dichromate actually was the major substance of commerce and should be the compound considered for test. He said that Lead Chromate and Calcium Chromate have been shown to be carcinogenic in experimental animals. Dr. Gould discussed the various industrial uses of chromium.

Given the fact that several chromium compounds already have been shown to be carcinogenic, Dr. Wilcox wondered about the need to test Sodium Dichromate. Even if Sodium Dichromate was found to be carcinogenic, it would be difficult to confirm that it was the only active chromium compound in an occupational exposure situation. A discussion ensued regarding the relationship of solubility to carcinogenicity and to the appropriate route of exposure. Dr. Gregory noted that occupational exposure was much greater for the insoluble chromates than for the soluble ones. He suggested that the insoluble compounds are more likely to be carcinogenic. Dr. Nelson noted three major occupational exposure settings; i.e., mining, production of chromium compounds, and plating operations. An increased cancer rate has been most conclusively shown among workers associated with the production of chromium compounds.

Dr. Clayson suggested that the irritating properties of chromium may act as a cocarcinogen. He recommended that chromate be tested as a promoter in the lung, as well as a complete carcinogen. Dr. Nelson opined that under the right conditions (e.g., alkalinity, persistence, and exposure time), Sodium Dichromate probably would be carcinogenic. He viewed the issue as more of a quantitative problem than a qualitative one.

On a linear (1 to 10) scale of progressive priority, Sodium Dichromate received a mean testing score of 3.3.

Cobalt and Cobalt Sulfate. Dr. Sevin said that Cobalt comes primarily from Africa and its processing is confined to one facility in the U.S. Production workers may be exposed to a variety of Cobalt and Nickel

salts. Dr. Sevin described the major usages of Cobalt and Cobalt Sulfate and areas of potential human exposure. Occupational exposure occurs mainly through inhalation. Cobalt was reported to produce local sarcomas in rats following intramuscular or intrathoracic injections. No carcinogenicity studies were found on Cobalt Sulfate. Dr. Sevin mentioned several disease conditions associated with Cobalt exposure.

Dr. Ray questioned the need to test both Cobalt and Cobalt Sulfate for carcinogenicity. He recommended that Cobalt be given a moderate testing priority. Dr. Wilcox suggested that Cobalt salts may be of most interest because of their solubility.

On a linear (1 to 10) scale of progressive priority, Cobalt received a mean testing score of 6.2 and Cobalt Sulfate a mean testing score of 5.0.

TEXTILE SPECIALTY CLASS

Stearatochromic Chloride Complex. Although the compound was identified during the review of textile chemicals, Dr. Weisburger said its most appreciable use was as a food packaging material. Despite its production, no human or animal data were found on its potential health effects. Stearatochromic Chloride Complex was selected by the CSWG with moderate priority.

Dr. Nelson noted the possibility of Stearatochromic Chloride Complex contaminating food. He indicated that it should receive a "middle" priority given the lack of information on its potential hazard. Dr. Ray suggested the compound be tested in a battery of short-term tests.

Regarding the approved use of Stearatochromic Chloride Complex by FDA, Dr. Siu said that migration would have to be virtually zero from the packaging material into the food. He cautioned that it was important to examine the specific approved uses of the compound. Dr. Clayson commented that the relative priority given to the chemical would depend upon whether the substance contaminated foods.

On a linear (1 to 10) scale of progressive priority, Stearatochromic Chloride Complex received a mean testing score of 1.3.

PLASTICIZERS

Tricresyl Phosphate. Dr. Cameron said that Tricresyl Phosphate was selected as a representative aryl phosphate based on its high production. He reviewed the various usages of the substance. Tricresyl Phosphate was reported not to be mutagenic in the Ames assay. Dr. Cameron noted that the compound was recommended for testing to the EPA by the TSCA Interagency Testing Committee. Tricresyl Phosphate was selected by the CSWG with low priority .

Based mainly on production volume, Dr. Ray suggested that Tricresyl Phosphate receive a medium to low priority for testing. Dr. Wilcox agreed to a moderately low priority.

On a linear (1 to 10) scale of progressive priority, Tricresyl Phosphate received a mean testing score of 2.3.

Tri(2-chloroethyl)phosphate. Dr. Cameron commented on the production and usages of Tri(2-chloroethyl)phosphate. The compound was selected from among the alkyl phosphates and given a moderate priority by the CSWG. Tri(2-chloroethyl)phosphate was selected based on the fact that it is an environmental contaminant and structurally related to the carcinogen, Tris(2,3-dibromopropyl)phosphate.

Although the substance has been detected as an environmental contaminant in fish, Dr. Wilcox said there were no data as to how widespread or serious was the problem. He recommended a moderate testing priority. Dr. Ray noted that Tri(2-chloroethyl)phosphate was inactive in the Ames assays, unlike Tris(2,3-dibromopropyl)phosphate. He suggested a low testing priority be given to the compound.

On a linear (1 to 10) scale of progressive priority, Tri(2-chloroethyl)-phosphate received a mean testing score of 2.3.

Neohesperidin Dihydrochalcone (Neo-DHC). Although he had had no dealing with the substance, Dr. Clayson abstained from the discussion on Neo-DHC because of his consulting activities related to artificial sweeteners. Dr. Nelson served as the Chairman for the Subgroup's discussio of Neo-DHC.

Dr. Kraybill said that Neo-DHC was a product obtained from the rind of citrus fruits. The USDA was particularly interested in it as a potential non-nutrient sweetener. Neo-DHC was found to be inactive in a two year carcinogenicity study in rats, sponsored by the USDA. Certain inadequacies in the study, however, limits its value. Dr. Kraybill said that Nutrilite, a commercial company interested in marketing Neo-DHC, was not in a position to support the additional long-term bioassay studies required by FDA. The CSWG selected Neo-DHC for testing in mice with a high priority.

Dr. Hays said that the USDA considered it to be in the public's best interest for the government to sponsor the necessary tests on Neo-DHC. Dr. Siu indicated that the FDA considered the USDA-rat study to be an inadequate test of Neo-DHC's carcinogenicity. He added that FDA had recommended to Nutrilite that carcinogenicity studies be undertaken in both the rat and mouse, as well as multi-generation reproductive and metabolism studies.

Because of the potential importance of the substance, Dr. Wilcox recommended that additional carcinogenicity studies be done in both rats and mice. Dr. Nelson said that a total toxicologic evaluation of Neo-DHC should be undertaken, including a multi-generation carcinogenicity study. He recommended that Neo-DHC be given a high testing priority.

A discussion ensued as to the appropriateness of the government supporting studies on a substance of commercial value. Dr. Ray opined that industry should bear the cost of such testing. A question arose regarding the patentability of the process by which Neo-DHC is derived. The Subgroup members generally agreed that, on scientific grounds, Neo-DHC should be tested; the decision as to who should pay for the tests being made by the appropriate government officials. Dr. Griesemer indicated that the question of financial responsibility would be considered when Neo-DHC is brought before the National Toxicology Program.

On a linear (1 to 10) scale of progressive priority, Neo-DHC received a mean testing score of 6.1. A motion was approved indicating that the Subgroup rating was based on the need to test Neo-DHC and did not concern financial responsibility for testing. Dr. Ray abstained from the vote and Dr. Clayson disqualified himself.

IV National Toxicology Program

Dr. Griesemer described the activities of the National Toxicology Program (NTP), particularly with respect to chemical selection. He briefly commented on the principles used by the NTP for chemical selection and on the types of substances and circumstances considered in making selections. He noted that industry would bear the responsibility for testing whenever possible.

Each of the eight NTP member agencies nominate chemicals. A coordinating group assembles the information, which is then reviewed by a NTP Chemical Nomination Group. Testing recommendations are made for all relevant toxicologic end-points and a priority rank assigned to each chemical. The final recommendations and priorities are submitted to the NTP Executive Committee for approval. Responsibility for testing resides with the NTP Director.

Experimental designs and specific types of tests are developed based on the needs of the individual agencies. After the appropriate tests have been identified and developed, the chemical is again submitted to the Executive Committee for approval. Dr. Griesemer commented on the various types of tests that could be undertaken.

Dr. Griesemer suggested that the Clearinghouse Chemical Selection Subgroup would be most useful in continuing to nominate chemicals

for carcinogenicity studies. He added that reviewing chemicals by classes was particularly advantageous since the interests of most of the other agencies were more restricted. The identification of research problems also would be a useful function of the Subgroup.

Dr. Clayson noted that one attraction of the Clearinghouse is that it is the only chemical selection group that meets in public sessions. Dr. Griesemer emphasized the necessity to document the rationale for selections so that the Subgroup's concerns will be adequately considered. He noted that some of the Subgroup's nominations may not be tested by the NTP because attempts will be made to have industry sponsor the testing. It was suggested that the Subgroup be kept informed of how its selections are fairing vis-à-vis nominations from other agencies.

As there was no further business, Dr. Clayson adjourned the meeting.

James M. Sontag, Ph.D.
Executive Secretary

ATTACHMENT 1

Priority Ranking

Shown below is the numerical ranking given by the Clearinghouse Chemical Selection Subgroup to those chemicals scored since November 1977. The ranking was done using a linear (1 to 10) scale of progressive priority. The final score of a particular chemical represents the aritmetic mean of the Subgroup members present and casting votes.

SUBSTANCE	SCORE
Isoproterenol Hydrochloride (CAS No. 51309)	8.7
Hydrochlorothiazide (CAS No. 58935)	8.3
Tetracycline Hydrochloride (CAS No. 64755)	8.3
Cadmium Oxide (CAS No. 1306190)	8.2
Nitrofurazone (CAS No. 59870)	8.2
Phenylephrine Hydrochloride (CAS No, 61767)	8.2
Dichlorvos (CAS No. 62737)	8.0
Diphenhydramine Hydrochloride (Benadryl^{R}) (CAS No. 147240)	8.0
Furosemide (CAS No. 54319)	8.0
Nickel Sulfate (CAS No. 7786814)	8.0
Phenolphthalein (CAS No. 77098)	7.7
Ampicillin (Amcill^{R}) (CAS No. 69534)	7.4
Cadmium Nitrate (CAS No. 10325947)	7.4
Chloramine (CAS No. 10599903)	7.2
Ephedrine (CAS No. 299243)	7.2
Nickel Oxide (CAS No. 1313991)	7.2
Phenytoin Sodium (CAS No. 630933)	7.2
Probenecid (Benemid^{R}) (CAS No. 57669)	7.2
Chlorpromazine (CAS No. 50533)	7.0
1,2-Epoxybutane (CAS No. 106887)	7.0
Glycidol (CAS No. 556525)	7.0
4-Hydroxyacetanilide (CAS No. 103902)	7.0
Methapyrilene (CAS No. 91805)	7.0
N-Nitrosodiethanolamine (CAS No. 1116547)	7.0
Picloram (CAS No. 1918021)	7.0
Benzathine Penicillin G (Bicillin^{R}) (CAS No. 1538096)	6.8
Epinephrine (CAS No. 51434)	6.8
Cinnamaldehyde (CAS No. 104552)	6.7
6-Methylcoumarin (CAS No. 92488)	6.7
Tetranitromethane (CAS No. 509148)	6.6
2,3-Dibromo-1-propanol (CAS No. 96139)	6.5
2-Amino-4-nitrophenol (CAS No. 99570)	6.4
Rhodamine 6G (CAS No. 939388)	6.3
2-Butanone Peroxide (CAS No. 1338234)	6.2
Carisprodol (Soma^{R}) (CAS No. 78444)	6.2
Cobalt (CAS No. 7440484)	6.2
Hexamethyl-*p*-rosaniline Chloride (CAS No. 548629)	6.2

Triamterene (CAS No. 396010)	6.2
Neohesperidin Dihydrochalcone (CAS No. 20702776)	6.1
Quinidine (CAS No. 56542)	6.1
2-Amino-5-nitrophenol (CAS No. 121880)	6.0
cis-Dichlorodiamine Platinum (II) (CAS No. 15663271)	6.0
C.I. Pigment Red 3 (CAS No. 2425856)	6.0
Erythromycin (CAS No. 114078)	6.0
Gibberellic Acid (CAS No. 77065)	6.0
Hydroquinone (CAS No. 123319)	6.0
2-Mercaptobenzimidazole (CAS No. 583391)	6.0
Propantheline Bromide (Pro-Banthine^{R}) (CAS No. 50340)	6.0
p-Quinone (CAS No. 106514)	6.0
1-Amino-2,4-dibromoanthraquinone (CAS No. 81492)	5.7
Hexachlorocyclopentadiene (CAS No. 77474)	5.6
Hexylresorcinol (CAS No. 136776)	5.6
Benzaldehyde (CAS No. 100527)	5.5
Organidin (CAS No. 5634399)	5.5
Indomethacin (Indocin^{R}) (CAS No. 53861)	5.4
2,4,6-Trinitrotoluene (TNT) (CAS No. 118967)	5.4
Carvone (CAS No. 99490)	5.3
Azodicarbonamide (CAS No. 123773)	5.2
Benzofuran (CAS No. 271896)	5.2
Crotonaldehyde (CAS No. 4170303)	5.2
1,8-Dihydroxy-4,5-dinitroanthraquinone (CAS No. 81550)	5.2
Methylphenidate (Ritalin^{R}) (CAS No. 113451, 298559)	5.2
Butyraldehyde (CAS No. 123728)	5.0
C.I. Pigment Red 23 (CAS No. 6471494)	5.0
Cobalt Sulfate (CAS No. 10124433)	5.0
p-Nitroaniline (CAS No. 100016)	5.0
α-Methylbenzyl Alcohol (CAS No. 98851)	4.8
Wollanstonite (CAS No. 13983170)	4.8
Ethyl Bromide (CAS No. 74964)	4.7
Succinic Anhydride (CAS No. 108305)	4.7
Bromobenzene (CAS No. 108861)	4.5
p-Nitrophenol (CAS No. 100027)	4.4
Catechol (CAS No. 120809)	4.3
Chloramphenicol (CAS No. 56756)	4.3
C.I. Pigment Yellow 74 (CAS No. 6358312)	4.3
Manganese Sulfate (CAS No. 7785877, 10124557)	4.3
Zirconium Oxychloride (CAS No. 7699436)	4.3
Furfural (CAS No. 98011)	4.2
N-Isopropyl-N'-phenyl-p-phenylenediamine (CAS No. 101724)	4.2
2,6-Xylidine (CAS No. 87627)	4.2
Acetaldehyde (CAS No. 75070)	4.1
Amphetamine (CAS No. 60151)	4.1
N-(1,3-Dimethylbutyl)-N'-phenyl-p-phenylenediamine (CAS No. 793248)	4.1
Sodium Selenite (CAS No. 10102188)	4.1

d-Limonene (CAS No. 5989275)	4.0
N,N'-Bis-(1,4-dimethylpentyl)-p-phenylenediamine (CAS No. 3081149)	4.0
γ-Butyrolactone (CAS No. 96480)	4.0
Benzyl Alcohol (CAS No. 100516)	3.8
Methyldopa (CAS No. 555306)	3.8
Nalidixic Acid (Neg Gram^{R}) (CAS No. 389082)	3.8
Sodium Aluminosilicate (CAS No. 1344009)	3.8
Hematoxylin (CAS No. 517282)	3.7
Furan (CAS No. 110009)	3.6
2,2-Bis(bromomethyl)-1,3-propanediol (CAS No. 3296900)	3.3
2,4-Dinitroaniline (CAS No. 97029)	3.3
Isophorone (CAS No. 78591)	3.3
Sodium Dichromate (CAS No. 10588019)	3.3
Citral (CAS No. 5392405)	3.2
Dimethoxane (CAS No. 828002)	3.2
Furfuryl Alcohol (CAS No. 98000)	3.2
Nickel Dust	3.2
Papaverine Hydrochloride (Pavabiod^{R}) (CAS No. 61256)	3.2
Pentaerythritol Tetranitrate (CAS No. 78115)	3.2
Polyvinyl Chloride Latex (CAS No. 9002862)	3.2
Ferroselenium (CAS No. 11108706)	3.1
Primaclone (Mysoline^{R}) (CAS No. 125337)	3.1
β-Cadinene (CAS No. 523477)	3.0
Dimethyloldihydroxyethyleneurea (CAS No. 1854268)	3.0
N-Methylolacrylamide (CAS No. 924425)	3.0
Amobarbital Sodium (CAS No. 64437)	2.8
1,2-Epoxyhexadecane (CAS No. 7320378)	2.8
3,4-Dihydrocoumarin (CAS No. 119846)	2.7
Diatriazoate Dosium (CAS No. 737315)	2.6
1-(2H)-Phthalazinone (CAS No. 119391)	2.6
Cyclandelate (CAS No. 456597)	2.5
p-Dibromobenzene (CAS No. 106376)	2.5
1,3-Dibromopropane (CAS No. 109648)	2.5
2-Amino-6-nitrobenzothiazole (CAS No. 6285570)	2.4
4-Chloro-2-nitroaniline (CAS No. 89634)	2.4
HC Yellow No. 4 (CAS No. 52551674)	2.4
o-Nitroanisole (CAS No. 91236)	2.4
1-((4-Nitrophenyl)azo)-2-naphthalenamine (CAS No. 3025772)	2.3
Tri(2-Chloroethyl)phosphate (CAS No. 115986)	2.3
Tricresyl Phosphate (CAS No. 1330785)	2.3
Isobutyraldehyde (CAS No. 78842)	2.2
Isosorbide Dinitrate (CAS No. 87332)	2.2
Nonanal (CAS No. 124196)	2.2
Selenium CAS No. 7782492)	2.2
p-Toluenesulfonyl Hydrazide (CAS No. 1576358)	2.2
Propionaldehyde (CAS No. 123386)	2.1
Methylcarbamate (CAS No. 598550)	2.0
1-trans-Δ^{9}-Tetrahydrocannabinol (CAS No. 1972083)	2.0
2,4,5-Trihydroxybutyrophenone (CAS No. 1421632)	2.0

Chlorinated Trisodium Phosphate (CAS No. 56802994)	1.7
Oxymetholone (CAS No. 434071)	1.6
2-(Aminomethyl)furan (CAS No. 617890)	1.4
4-Aminopyridine (CAS No. 504245)	1.3
Stearatochromic Chloride Complex (CAS No. 15242963)	1.3
Diethyl Carbonate (CAS No. 105588)	1.2
Titanium (CAS No. 7440326)	1.2
n-Dodecylmercaptan (CAS No. 112550)	1.1
Chromated Copper Arsenate (CAS No. 37337136)	1.0
EDTA (CAS No. 64028)	1.0
Isopropanol (CAS No. 67630)	0.8

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8/15/79

ChemRisk/Shonka Research Associates, Inc., Document Request Form

From Box 12-2-3-16

(This section to be completed by subcontractor requesting document)

J. Lamb / 1034A
Requestor / Document Center (is requested to provide the following document)

Date of request ~~12/8/95~~ 1/96 Expected receipt of document 1/8/95

Document number _____ Date of document 1/31/80

Title and author (if document is unnumbered) (5 documents)

Rel (1) Updated Study of DOE-UCC/ND Nickel Workers at K-25
and attachment (C C Lushbaugh) DRAU, 1/31/80

CO (2) Attachment to Item 1 – Letter to S S Stuf from A Warner, Inco Limited, dated 3/7/80

(This section to be completed by Document Center)

Date request received 1/22/96

Date submitted to ADC 1/25/96

Date submitted to HSA Coordinator 1/22/96

(This section to be completed by HSA Coordinator)

Date submitted to CICO 1/25/96

Date received from CICO 3/4/96

Date submitted to ChemRisk/Shonka and DOE 3/4/96

(This section to be completed by ChemRisk/Shonka Research Associates, Inc.)

Date document received _____

Signature _____

Rel (3) Letter to LA Dean et al., from J A Barker, dated 12/21/79, A Long-Term Mortality Study of ORGDP Barrier Workers Exposed to Metallic Nickel (W/O Attachment)

CO (4) Letter to Ad Hoc Inorganic Nickel Committee & Dr. K. Lane dated 8/15/79, from D L Hazzies, Chemical Selection ~~of~~ Subgroup of the Clearinghouse on Environ. Carcinogens. Mtg May 25, 1979 (W/O Attach)

CO (5) Attachment to Item 4, Dept of HEW, Minutes, fifteenth Mtg of Chemical...

J. Stuart Warner
Vice-President

March 7, 1980

Mr. Stan S. Stief
Union Carbide Corporation
Nuclear Division
Building K-1001, Mail Stop 141
P.O. Box P
Oak Ridge, Tenn 37830

Dear Stan:

You have received copies of the letter and the summary table of epidemiologic studies that I sent to OSHA's Docket Officer on December 21, 1979. The submission simply requested that OSHA consider these studies when developing its schedule for the revised nickel standard. At the same time, I asked Dr. Bailus Walker, OSHA's Director of Health Standards Programs, to meet with me to discuss timing and other matters related to the nickel standard. This letter is to inform you what I learned at that meeting and what I think we should do about it.

Dr. Walker, seven members of his staff and one person from NIOSH met with one of my colleagues and me on February 7, 1980. See the attached page for attendees. The meeting lasted about three hours; Dr. Walker was present for nearly two hours. We discussed a number of topics -- some repeatedly -- and continually emphasized that industry had been and would continue to be helpful. The following headings summarize topics of interest.

Approach to Rulemaking

OSHA made clear its intention to use the recently promulgated OSHA Cancer Policy to revise its occupational exposure standard for nickel. I asked if they would consider a traditional 6(b) rulemaking while the OSHA Cancer Policy (OCP) was being reviewed by the court. Dr. Walker said they did not plan to do so.

If you have not already done so, I suggest you obtain a copy of the OCP (Federal Register, Tuesday, January 22, 1980, pp. 5001-5296) and slug your way through it. Unless the court invalidates all or portions of the policy, these are the rules under which a nickel standard will be developed. You will find them to be very restrictive.

/...

OSHA is now preparing its "Candidate List" of potential occupational carcinogens for publication by July 1, 1980. They are also developing two lists of approximately 10 substances each which are candidates for rulemaking as Category I and Category II Potential Carcinogens respectively. Rumor and gut feeling indicate nickel is on the Category I priority list but Dr. Walker refused to comment on this.

Just when rulemaking will begin depends mainly on what the Court does to the OCP but also on the manpower OSHA can devote to a nickel standard. OSHA still hopes to propose a nickel standard this summer. Dr. Walker would make no commitment to delay this event until the end of 1980 to permit completing the epidemiologic studies. I argued that these results would be invaluable to OSHA but he would not yield. If you are the sponsor of an unfinished epidemiologic study, I urge you strongly to keep after your consultant to complete it as soon as possible!

Non-positive Epidemiologic Studies

Dr. Walker asked what we expected our epidemiologic studies would show. I said we hoped they would show that the increased incidence of respiratory cancer seen at times in the past was in fact confined to certain refinery operations in the nickel-producing industry. If true, many of these studies would produce so-called "non-positive results".

Unfortunately, the OSHA Cancer Policy states that the Secretary of OSHA will not even consider evidence showing a non-positive result unless it meets the following criteria:

(i) *The epidemiologic study involved at least 20 years' exposure of a group of subjects to the substance and at least 30 years' observation of the subjects after initial exposure;*

(ii) *Documented reasons are provided for predicting the site(s) at which the substance would induce cancer if it were carcinogenic in humans; and*

(iii) *The group of exposed subjects was large enough for an increase in cancer incidence of 50% above that in unexposed controls to have been detected at any of the predicted sites.*

/...

Your consulting epidemiologist will tell you that the first and third criteria are difficult if not impossible to meet, particularly simultaneously. I returned to this subject several times in the course of the afternoon but made no progress. Dr. Infante explained the weakness of epidemiologic studies as evidence that something is not a carcinogen. I assured them we understand that such studies require careful evaluation but that we could not understand rigid adherence to the arbitrarily chosen criteria of 20 years exposure and 30 years follow-up. Under these rules, a plant that had been in operation for 29 years could not even have its study accepted for evaluation -- unless of course, it showed there was a cancer hazard! I argued that the studies should at least be evaluated.

Please don't be too discouraged. We at Inco intend to complete our studies simply because we believe there are useful things to be learned from them. Furthermore, the court may make OSHA behave more flexibly as I believe OSHA's present position is not in compliance with section 6(b)(5) of the OSH Act.

However, there is a warning here that your epidemiologist should consider when analyzing data and writing reports. I think he or she must compare groups of employees with varying lengths of exposure and of follow-up to look for trends (or the absence of trends) as the years of exposure and follow-up approach the OSHA criteria of 20 and 30 years respectively. If possible, he or she should isolate a group that meets the first OSHA criteria even if it is too small to meet the third one. Dr. Infante is particularly interested in seeing what fraction of total man-years at risk is contributed by groups with long exposure and follow-up.

I will make available some data on latency periods from circumstances in which there clearly was an occupational hazard. Your consultant might be able to use these to decide at how much less than 30 years latency an increased incidence of cancer might have been expected to appear -- if it existed. We may eventually be able to provide some data indicating that exposures of considerably less than 20 years were sufficient to put an exposed person at risk in certain circumstances. If your consultant has some ideas for coping with OSHA's present position, I hope he or she will share them with the rest of us.

"Inorganic Nickel"

We asked if OSHA intended to regulate "inorganic nickel" as a substance or whether they would examine nickel and its compounds one at a time. They said this had not yet been decided.

/...

I pointed out that OSHA was considering regulating the insoluble compounds of one valence state of chromium, a rather fine subdivision. I suggested OSHA consider nickel in at least four different categories: metal and alloys; oxides; soluble salts; and insoluble compounds such as Ni_3S_2. They seemed interested to learn that many plants could rule out the presence of certain of these classes of nickel-containing substances.

I also inquired whether OSHA was considering establishing different permissible exposure limits for different industrial operations as they had done for cotton dust. OSHA had no comment. I pointed out the vast difference between controlling emissions from a plating bath and from a Pierce-Smith converter. I hope Radian will lead OSHA to think along these lines.

Regulatory Analysis

Last October, OSHA contracted with Radian to conduct a Phase I study to gather the information needed for a regulatory analysis. The contract covered only two industry groups -- primary producers and stainless-steelmakers. We have been explaining for some time that this was totally inadequate coverage of a large and complex industry.

To our delight, we were told that the scope of Radian's charter had been greatly increased. To our dismay, we later learned the funds available to Radian will be increased from $80,000 to only $90,000. The increase is totally inadequate.

This simply means that if Radian asks for information we should be as helpful as possible. If you have information you think Radian would find useful, I hope you will volunteer it if Radian doesn't approach you soon. Their report is due by June 30th so they will probably need to have all their data in hand by the end of April.

Contacts

Several people present expressed interest in particular kinds of data. They would be happy to serve as contact people at least until a nickel project officer is designated.

Epidemiology - Dr. Infante

Engineering feasibility - Drs. Hanna and Cram. One of the staff volunteered that Dr. Cram, a new OSHA employee, may be given the nickel project. This was not confirmed. (It may be pure cir-

/...

cumstance but it worries me that Cram is a chemical engineer. It could mean OSHA feels all the health questions about nickel have been answered and that the only remaining questions are about technical feasibility.)

In vitro studies	-	Dr. Susan Harwood (not present)
Animal studies	-	Dr. Harwood and Dr. Patricia Marlowe (not present)
Economic studies	-	Cindy Bascetta

Plant Visits

Several members of OSHA's staff said they needed to learn more about the industry and would like to make some plant visits. We encouraged them to do so. We have invited them to visit our Canadian production facilities and our Dr. Schaller is trying to set up an efficient tour of nickel-consuming operations in the U.S. I hope you will cooperate with him if he should ask you to host a visit.

Sincerely,

Stuart

JSW:jm
attach

ATTENDEES AT FEBRUARY 7, 1980 MEETING
WITH OSHA CONCERNING THE NICKEL STANDARD

OSHA		
Dr. Bailus Walker	Director, Health Standards Programs	(202)-523-7076
Dr. Fayez Hanna	Director, Office of Toxic Substances	(202)-523-7075
Dr. Peter Infante	Director, Office of Carcinogen Identification & Classification	(202)-523-7111
Dr. Han K. Kang	Health Scientist, Office of Carcinogen Identif. and Classif.	(202)-357-0325
Mr. Barrett Fountos	Health Scientist, Office of Carcinogen Identif. and Classif.	(202)-357-0325
Dr. Kenneth Cram	Chemical Engineer, Office of Carcinogen Standards	(202)-523-7147
Mr. Robert Manware	Industrial Hygienist, Office of Carcinogen Standards	(202)-523-7148
Ms. Cynthia Bascetta	Economist, Office of Regulatory Analysis	(202)-523-7056
NIOSH		
Dr. Imogene Sevin	Priorities Research and Analysis Branch	(301)-443-2100
INCO		
Mr. Samuel Goldberg	Inco United States, Inc.; Vice-President	(212)-742-4538
Dr. Stuart Warner	Inco Limited; Vice-President	(416)-361-7866

Box #15-1-41

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(Box 4)

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Date of request 6/28/96 Expected receipt of document _____

Document number ~~EM-467~~ Date of document 7/11/96

Title and author (if document is unnumbered)

Sanitized Version of IH Investigation of Health Hazards

(This section to be completed by Document Center)

Date request received 7/1/96

Date submitted to ADC 7/11/96

Date submitted to HSA Coordinator 7/1/96

(This section to be completed by HSA Coordinator)

Date submitted to CICO 7/11/96 7/29/96

Date received from CICO 7/22/96

Date submitted to ChemRisk/Shonka and DOE _____

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Date document received _____

Signature _____

K/EM-467

SANITIZED VERSION OF IH INVESTIGATION OF HEALTH HAZARDS

(Sanitized Version of Unnumbered CRD Document)

Compiled by
S. G. Thornton
Environmental Management Division
OAK RIDGE K-25 SITE
for the Health Studies Agreement

July 11, 1996

Oak Ridge K-25 Site
Oak Ridge, Tennessee 37831-7314
managed by
LOCKHEED MARTIN ENERGY SYSTEMS, INC.
for the U.S. DEPARTMENT OF ENERGY
under Contract DE-AC05-84OR21400

110.6

INTER-COMPANY CORRESPONDENCE

UNION CARBIDE NUCLEAR COMPANY

A Division of Union Carbide and Carbon Corporation

To: Dr. J. S. Lyon

Plant: ORGDP

Date: April 10, 1959

Copies To: D. L. Stoddard
File-RC

Subject: Industrial Hygiene Investigation of Health Hazards

On April 6, 1959, Mr. _____ was seen in the ORGDP Dispensary with a complaint of nasal blockage, allegedly due to working with _____. Examination showed acute nasal mucous membrane irritation, nasal discharge and edema. Sinus X-rays showed minimal involvement. It was also learned that others working with the compound had had some complaints.

It was obvious that Mr. _____ had an acute rhinitis. Four possibilities presented themselves: (1) A simple rhinitis coincidental to working _____, (2) an individual allergy _____, (3) heavy dust loading of the atmosphere with secondary aggrevation of a pre-existing sinusites or (4) that _____ was a respiratory irritant. A simple rhinitis was unlikely because of the history of exacerbation of symptoms _____. Skin test with the material _____ to determine allergy were all negative and thus tended to rule out allergy as the cause.

Since there is a possibility that the use of this compound will be adopted in regular plant operations, it was felt that the health hazards from this material should be evaluated.

is no information in the literature so an independent investigation was required.

It was found that 24 employees had worked with . If a serious respiratory irritant, it can be assumed that it would cause more visits of these employees to the dispensary for respiratory symptons. The individual records were each checked for the number of visits and revisits for respiratory complaints during the period of January 1, 1959 to March 31, 1959. During this time there were 11 initial visits and 4 revisits for respiratory complaints, a total of 15 visits from this group over a three-month period. The number of visits and revisits from these employees for respiratory complaints during the period January 1, 1958 to March 31, 1958 was used as a control. During this time there were 10 initial visits and 7 revisits for respiratory complaints, giving a total of 17 visits for the three-month control period. There is obviously no difference between the number of dispensary visits during the control period and the period during which the employees were working

The twenty-four employees were then called in and interviewed individually as to any "symptoms" noted This type

of study is certainly biased, but each employee seemed to try to make an honest appraisal.. The results are as follows:

(1) Sixteen (67%) noted some evidence of upper respiratory irritation indicated by sneezing, sinus drainage, sensation of irritation and in a few cases blood spotting of nasal secretions.

(2) Four (17%) had chest symptoms of coughing or soreness. None were sure that this was due to any exposure.

(3) Twenty (83%) indicated slight skin irritation evidenced by dryness. pruritis, redness or slight rash. The use of hand lotions was effective in clearing the dryness.

Air analyses taken in the work area indicate that the dust load and dust count under normal operating conditions are so low that a non-irritating dust would cause no symptoms in the average employee. Unfortunately, we have no dust counts made in the early stages of this operation when ventilation was inadequate and spills more frequent.

Conclusions:

A study such as this can give no accurate data from which definite conclusions can be drawn. The best calculated opinions at which I can arrive are as follows:

(1)

(2)

(3)

(4)

Recommendations:

(1) Provide adequate ventilation or closed systems in the area in

(2) Use of gloves in handling this material. Protective creams might serve the same purpose, but these have not been evaluated.

(3) Use of care, and if possible, a closed system, in operations requiring dumping or loading of this material.

(4) If adequate ventilation or closed system are provided, there is no need for use of respiratory. Dumping and loading may require the use of respirators.

(5) Reassurance of all concerned that there is no indication that this material is a serious health hazard.

T. L. Ray, M.D.

TLR:nrd